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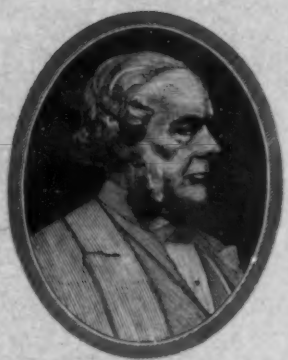

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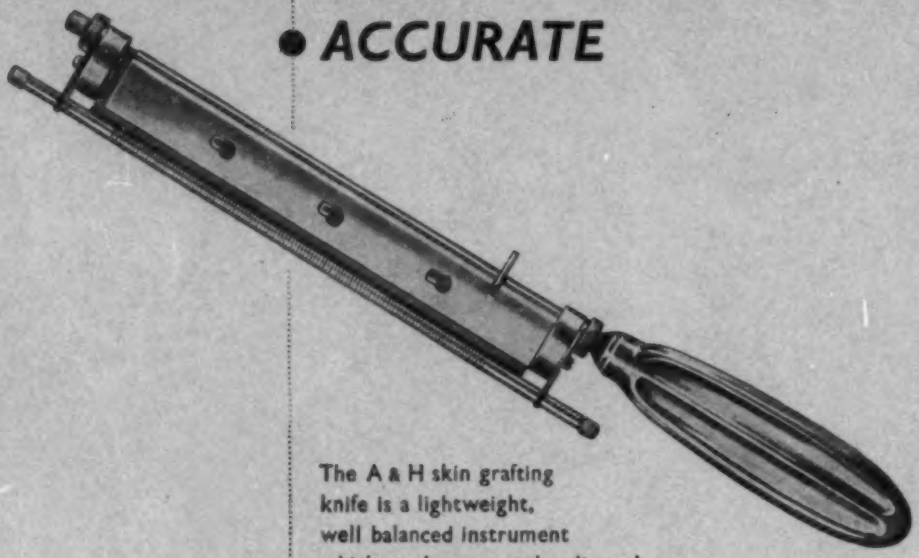

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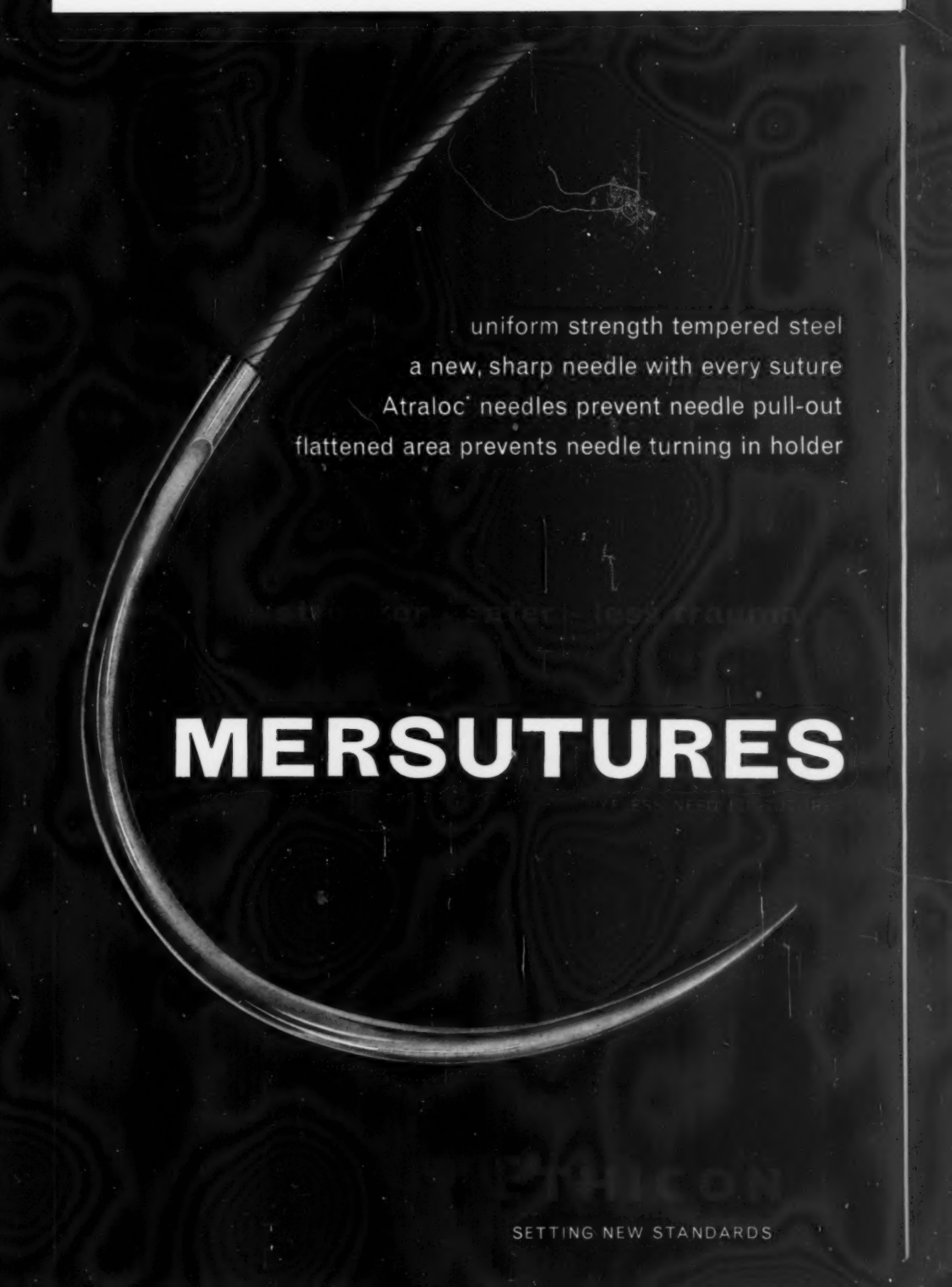
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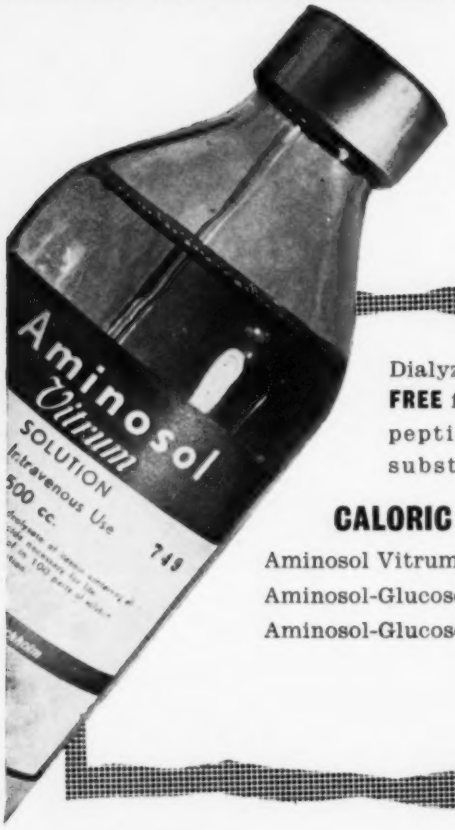

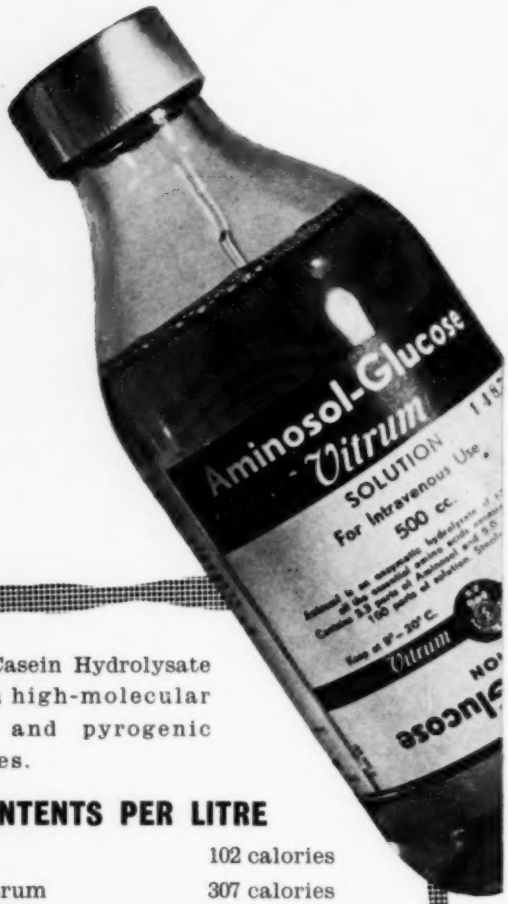

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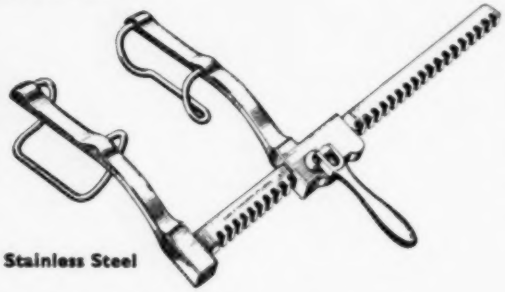

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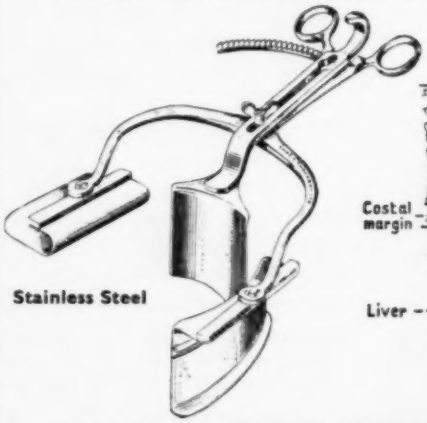

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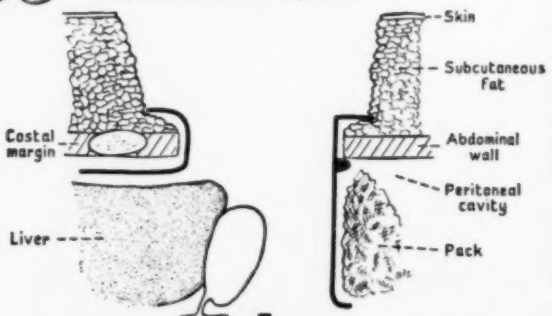

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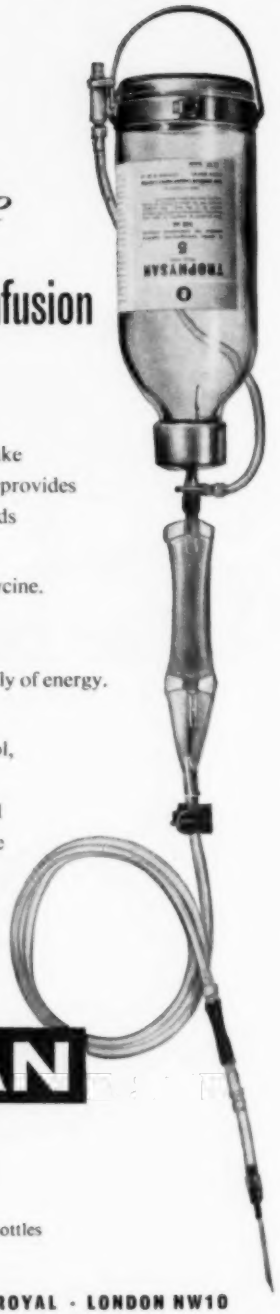

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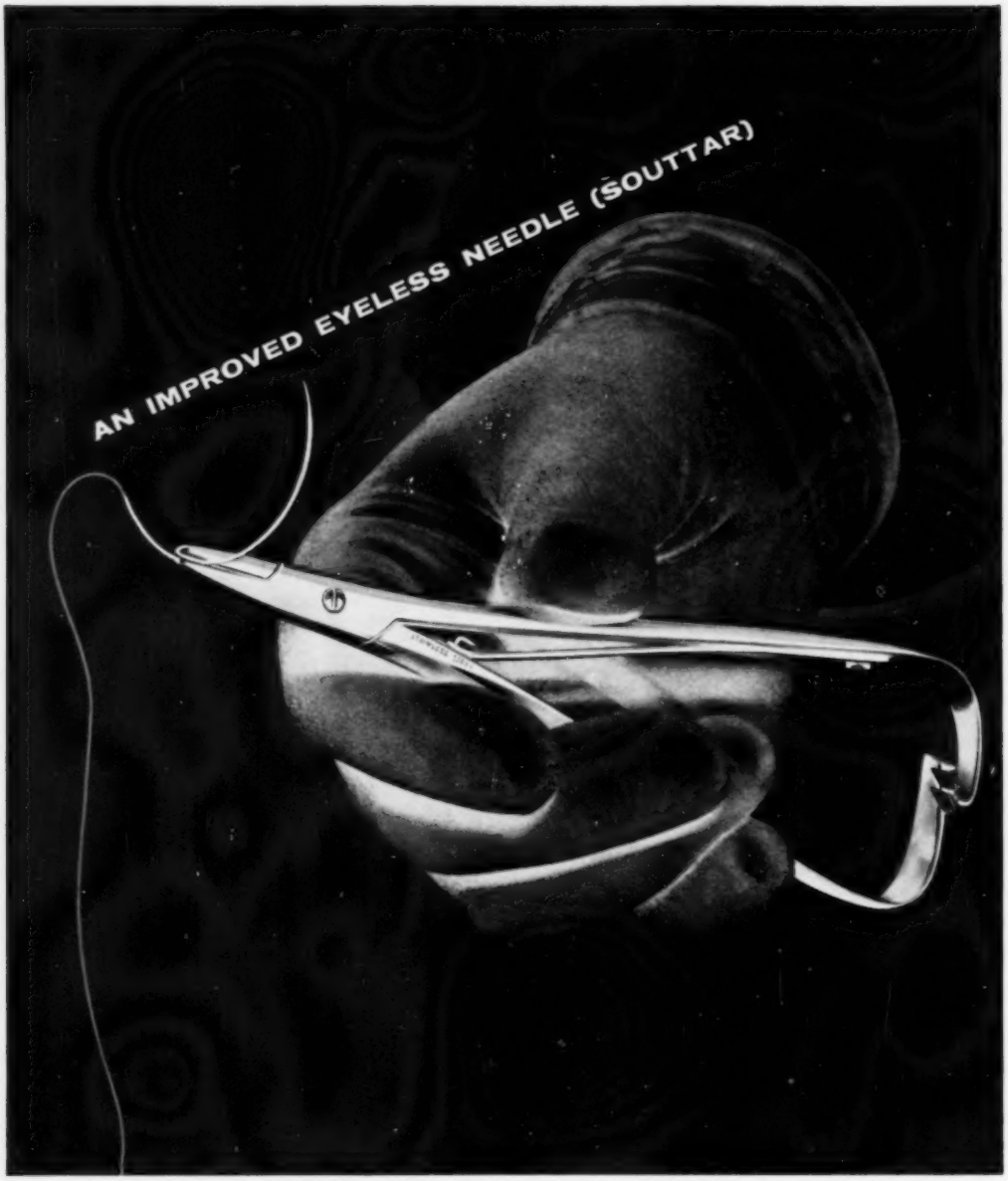

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THE DEVELOPMENT OF CARCINOMA OF THE LARGE INTESTINE IN ULCERATIVE COLITIS

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THE development of large intestinal carcinoma in patients suffering from ulcerative colitis has been described by many authors since the first reported association of the two conditions by Crohn and Rosenberg in 1925. Various estimates of the incidence of large bowel cancer in ulcerative colitis have been given by different authors (reviewed by Goldgraber, Humphreys, Kirsner, and Palmer, 1958). For instance, Felsen and Wolarsky (1949) found no carcinoma in 855 patients whereas Wheelock and Warren (1955) reported 29 cases (8·8 per cent) in their study of 319 patients. Whether this is a causal relationship or mere chance association has been much discussed. There are two main approaches to the investigation of causal relationship in this problem; the one requires a careful statistical analysis of the findings in a large group of ulcerative colitis cases kept under constant review for many years, while the other involves a detailed pathological study of the colon in an attempt to differentiate a form of carcinoma peculiar to the large intestine in ulcerative colitis.

The present survey is based upon a study of 663 patients with ulcerative colitis who have attended the Gordon Hospital, London, in the eleven and three-quarter years up to December, 1958. We have been concerned both with the pathological approach to the problem and the analysis of certain features of the whole group of ulcerative colitis cases for comparison with those developing cancer of the large bowel.

METHODS OF STUDY

General Review of Ulcerative Colitis Patients.—The follow-up records of 735 patients with suspected colitis were examined and in 663 cases the diagnosis was considered proven. The final diagnosis of ulcerative colitis was based on proctoscopy, sigmoidoscopy, and the radiological appearances after barium enema. In 284 cases there was confirmation of ulcerative colitis by rectal or colonic biopsy, and in 183 a part or all of the colon was examined after resection at the Gordon Hospital.

The whole group of patients has been further analysed according to sex, age at onset of colitic symptoms, duration of symptoms up to December, 1958 or earlier death, the age of each patient at time of survey or death, and the extent of bowel involvement by the colitic process. This information was obtained as a means of assessing the general characteristics of the whole group of patients in whom the development of large bowel carcinoma was being studied.

Detailed Review of Ulcerative Colitis Cases developing Large Bowel Carcinoma.—Among the 663 patients studied 19 cases with carcinoma of the large bowel were found, giving a crude incidence of 2·9 per cent. These cases are described below from the clinical and pathological viewpoint (*see* Case Reports).

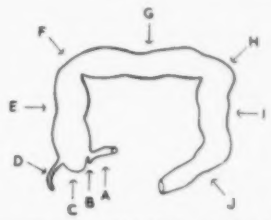


FIG. 122.—Sites from which blocks are taken in the routine examination of a resected colon. A, Terminal ileum; B, Ileocæcal valve; C, Cæcum; D, Appendix; E, Ascending colon; F, Hepatic flexure, G, Transverse colon; H, Splenic flexure; I, Descending colon; J, Sigmoid colon and sites of special interest.

Assessment of the Part of the Bowel involved in Ulcerative Colitis.—An attempt has been made to assess the extent of the colitis on clinical, radiological, sigmoidoscopic, and proctoscopic evidence, and in many cases histological material has also been available. Results are difficult to assess and the following grouping represents the best at present available in our series.

1. *Total Involvement.*—Radiological, sigmoidoscopic, and, in many cases, histological evidence of involvement of the whole large bowel.

2. *Subtotal or Partial Involvement.*—Sigmoidoscopic and often histological evidence of disease in the sigmoid colon and rectum with positive X-ray changes in the descending colon, but a normal radiological appearance in the ascending colon. The transverse colon may or may not be involved.

3. *Distal Involvement.*—Sigmoidoscopic and often biopsy evidence of disease in the sigmoid and rectum

with normal radiological appearances in the rest of the colon.

4. *Segmental Involvement.*—Sigmoidoscopic, radiological, and sometimes histological evidence of a patchy distribution of colitis with 'skip areas'.

5. *Indeterminate.*—A group of cases all of which have colitis but in which the precise extent is

FIG. 123.—A characteristic pseudopolyp showing surface mucosal erosion and inflammatory changes. Hæmatoxylin and eosin. (× 40.)

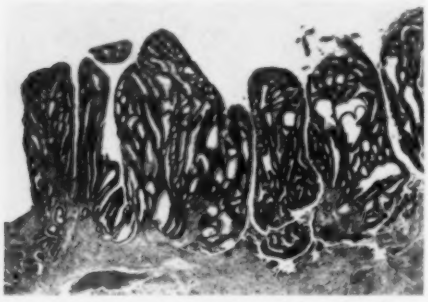


FIG. 125.—A characteristic papilloma of the colon. Hæmatoxylin and eosin. (× 20.)

undetermined. Many are still undergoing investigation and will later be assigned to one of the other groups.

When subsequent full histological examination of resected bowel has been possible the disease has in general been more widespread than the radiographic and sigmoidoscopic findings indicated. The figures given later for Groups 2–4 above will therefore represent a conservative estimate of the extent of bowel involvement.

Examination of Resected Lengths of Bowel.—The bowel is washed through with physiological saline, filled with 10 per cent formalin, and both ends clamped. It is then allowed to fix for twenty-four to forty-eight hours. After fixation it is bisected longitudinally; one half is used for photography and blocks for section are taken from the other half. In total colectomy specimens blocks are taken routinely from fixed zones (*Fig.* 122) as well as from areas of special interest. Lymph-nodes are dissected out from all regions suspected of having undergone malignant change.

FIG. 124.—A characteristic adenomatous polyp of the colon. Hæmatoxylin and eosin. (× 25.)

Histological Assessment of the Activity of the Colitic Process.—On the basis of 183 colectomy specimens we classify ulcerative colitis into three categories.

1. *Acute.*—Cases in which there is mucosal ulceration or erosion with inflammatory cellular infiltration, congestion, and œdema of the lamina propria and submucosa. Pseudopolyps are often present and there is little or no evidence of mucosal regeneration or fibrosis. Crypt abscesses and islands of 'buried' epithelium in the submucosa are often conspicuous.

2. *Chronic Active.*—Cases in which active lesions, as described above, are present in greater or lesser degree. There is evidence of repair in the form of regeneration of the surface mucosa and submucosal fibrosis which may be slight or considerable. Pseudopolyps are common.

3. *Quiescent.*—Cases in which signs of active inflammation are absent and the mucosa is either atrophic or replaced by fibrous tissue. Submucosal fibrosis is often extensive.

Most cases appear to progress from 1 through 2 to 3 but are subject to reactivation, with transition from the quiescent to the chronic active phase. Sometimes one part of the bowel shows an active lesion while another part is quiescent; such cases are classified as chronic active colitis.

Assessment of the Carcinoma.—The carcinoma has been classified as well differentiated, moderately differentiated, or poorly differentiated

(including anaplastic growths), and the presence or absence of mucus secretion has been noted. Individual features such as the relationship of carcinoma to stricture, 'buried' epithelium, and polyps are discussed below.

Assessment of Polypoid Lesions.—A study of 183 resected colons in ulcerative colitis has convinced us that the inflammatory pseudopolyps found in this condition are normally different and sharply separable from adenomatous polyps and papillomas which we regard as true neoplasms. In some of our cases, however, polypoid growths of intermediate type have occurred and the question of transition from one type to another arises. We have

Table I.—A Summary of the General Features in 19 Cases of Ulcerative Colitis with Large Bowel Carcinoma

Case No.	Sex	Age at Onset of Colitis Symptoms Years	Age at Diagnosis of Cancer Years	Duration of Colitis before Cancer diagnosed Years	Distribution of Colitis in Colon	Activity of Colitis in Colon	Site of Primary Cancer	Operative Treatment	Survival after Cancer diagnosed
1	M.	35	47	12	Total	Chronic active	Colon	Colectomy ileorectal anastomosis	7 yr. Dead
2	F.	20	28	8	Total	Chronic active	Transverse colon	Inoperable	12 d. Dead
3	F.	37	63	26	Total	Quiescent	Rectum	Inoperable	21 d. Dead
4	F.	20	45	25	Total	Quiescent	Rectum	Abdominoperineal excision	30 mth. Dead
5	F.	29	36	7	Partial	Chronic active	Rectum	Abdominoperineal excision	7 mth. Dead
6	M.	18	37	19	Uncertain	Chronic active	Sigmoid colon	Partial colectomy	9 mth. Dead
7	M.	49	51	2	Total	Chronic active	Transverse colon	Colectomy ileorectal anastomosis	4 yr. Alive
8	F.	12	31	19	Total	Chronic active	Rectum	Anterior resection	5 mth. Dead
9	F.	21	45	24	Total	Chronic active in colon (colectomy 7 yr. before)	Rectal stump	Inoperable (colectomy 7 yr. before)	10 d. Dead
10	F.	30	50	20	Total	Quiescent	Ascending and descending colon	Colectomy ileorectal anastomosis	18 mth. Dead
11	F.	28	52	24	Total	Chronic active	Colon	Colectomy ileorectal anastomosis	9 mth. Alive
12	F.	31	59	28	Uncertain	Chronic active	Rectum	Abdominoperineal excision	4 mth. Alive
13	F.	39	57	18	Total	Chronic, active	Cæcum	Colectomy ileorectal anastomosis	3 mth. Alive
14	M.	4	24	20	Total	*a*. Chronic active in colon colectomy 3 yr. before *b*. Quiescent in rectum at abdominoperineal excision	Rectum	Abdominoperineal excision. Colectomy with ileorectal anastomosis 3 yr. before	3 mth. Alive
15	F.	15	34	19	Partial	Quiescent	Rectum	Abdominoperineal excision	12 mth. Dead
16	M.	29	49	20	Uncertain	Quiescent	Rectum	Abdominoperineal excision	12 mth. Alive
17	M.	18	45	27	Distal	Uncertain	Rectum	Abdominoperineal excision and partial colectomy	13 mth. Dead
18	M.	28	33	5	Total	Chronic active	Uncertain	Inoperable	10 d. Dead
19	F.	33	47	14	Total	Chronic active	Uncertain	Inoperable	2 mth. Dead
Mean = S.E.M. = Range =		26·1 yr. 2·4 4–49	43·8 yr. 2·4 24–63	17·7 yr. 1·8 2–28					

therefore laid down criteria by which we separate inflammatory pseudopolyps from true neoplastic polyps and have discussed the intermediate forms. The criteria are given below.

Inflammatory pseudopolyps are of three types (*see also* Lumb and Protheroe, 1958):—

1. Short mucosal tags representing fragments of mucosa remaining after ulceration.

Table II.—Distribution of Ulcerative Colitis in the Whole Group and Carcinoma Group

Involvement	Whole Group (663 Cases)		Carcinoma Group (19 Cases)	
	Number	Percentage	Number	Percentage
Total	264	40	13	68*
Partial	225	34	2	11
Distal	104	16	1	5
Segmental	14	2	0	0
Indeterminate	56	8	3	16

* The high incidence of total colitis may be related to the fact that resected specimens were examined in all cases. The histological involvement is always more extensive than the clinical.

2. Granulomatous polyps consisting of granulation tissue usually devoid of mucosal covering.

3. Glandular elements surrounded by inflammatory tissue with varying degrees of surface mucosal erosion (*Fig.* 123). This group of polyps may show glandular hyperplasia of an orderly and regenerative type with the formation of dilated cystic gland spaces and much mucin (Coffey and Bargen, 1939).

Neoplastic polyps take the form of adenomas consisting of well differentiated glandular tissue without, as a rule, mucosal erosion or stromal inflammation (*Fig.* 124) and resembling normal colonic mucosa, or papillomas which have delicate connective tissue cores clothed by columnar epithelium (*Fig.* 125). Both are normally sharply separable from each other and from inflammatory pseudopolyps.

RESULTS

Case reports including clinical and pathological features of the 19 ulcerative colitis patients with large intestinal carcinoma are given on pp. 123–127; some of the important details of the cases are also given in *Tables I, II,* and *III*. In *Cases* 1–16 both the ulcerative colitis and the carcinoma were confirmed histologically, in *Case* 17 there was no histological confirmation of the colitis, while in *Cases* 18 and 19 the site of primary carcinoma was difficult to assess with certainty.

Age at Onset of Colitic Symptoms.—

Whole Group.—Accurate information was available in 648 of the 663 cases reviewed, and the average age at onset for the group was 35 years, irrespective of sex; the standard error of the mean (S.E.M.) was 2·5. *Fig.* 126 shows the distribution of the ages at onset in 5-year periods according to

Table III.—A Summary of the Pathological Features in 19 Cases of Ulcerative Colitis with Large Bowel Carcinoma

Case No.	Sex	Distribution of Ulcerative Colitis	Activity of Colitis	Site of Primary Carcinoma	Stricture Present	Histological Differentiation of Carcinoma	Mucus Secretion	Fibrous Stromal Reaction	Polyps Present and Type			Survival after Diagnosis of Carcinoma
									True	Pseudo	Transitional	
1	M.	Total	Chronic active	Colon	No	Well	None	No	Yes	No	No	7 yr. Dead
2	F.	Total	Chronic active	Colon	No	Poorly	+	No	No	No	No	12 d. Dead
3	F.	Total	Quiescent	Rectum	No	Poorly	+ + +	No	No	No	No	21 d. Dead
4	F.	Total	Quiescent	Rectum	No	Moderately	+	Yes	No	No	No	30 mth. Dead
5	F.	Partial	Chronic active	Rectum	Yes	Poorly	+ + +	Yes	Yes	Yes	Yes	7 mth. Dead
6	M.	Uncertain	Chronic active	Colon	Yes	Well	+	Yes	Yes	Yes	Yes	9 mth. Dead
7	M.	Total	Chronic active	Colon	Yes	Moderately	+ +	No	Yes	Yes	Yes	4 yr. Alive
8	F.	Total	Chronic active	Rectum	No	Moderately	None	Yes	Yes	No	No	5 mth. Dead
9	F.	Total	Chronic active	Rectum	Yes	Poorly	+ + +	No	No	No	No	10 d. Dead
10	F.	Total	Quiescent	Colon × 2	Yes	Moderately	+	Yes	Yes	Yes	Yes	18 mth. Dead
11	F.	Total	Chronic active	Colon	No	Well	None	Yes	Yes	No	No	9 mth. Alive
12	F.	Uncertain	Chronic active	Rectum	No	Moderately	+ +	No	Yes	Yes	Yes	4 mth. Alive
13	F.	Total	Chronic active	Cæcum	Yes	Moderately	None	No	Yes	Yes	Yes	3 mth. Alive
14	M.	Total	Quiescent	Rectum	No	Moderately	+ +	Yes	No	No	No	3 mth. Alive
15	F.	Partial	Quiescent	Rectum	No	Poorly	+ + +	No	No	No	No	12 mth. Dead
16	M.	Uncertain	Quiescent	Rectum	Not known	Well	None	Yes	No	No	No	12 mth. Alive
17	M.	Distal	Uncertain	Rectum	Not known	Poorly	None	No	No	No	No	13 mth. Dead
18	M.	Total	Chronic active	Uncertain	No	Poorly	+ +	—	—	—	—	10 d. Dead
19	F.	Total	Chronic active	Uncertain	Yes	—	—	—	—	—	—	2 mth. Dead

sex. It can be seen that 275 patients (41·5 per cent) were less than 31 years of age at the onset of their disease and that 82 patients (12·6 per cent) were less than 21 years old.

Carcinoma Group.—In these 19 patients the average age at onset of symptoms was 26·1 years (S.E.M. = 2·4). Thirteen patients (68·5 per cent) were less than 31 years old and 7 (36·8 per cent) were less than 21 years of age.

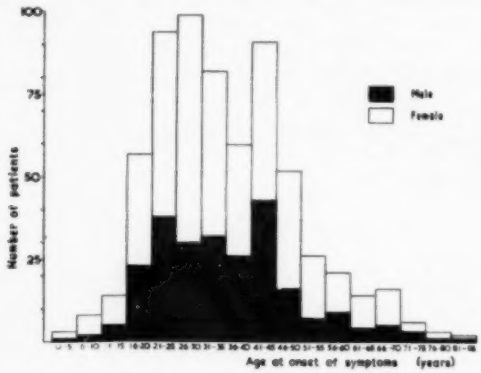


FIG. 126.—Age at onset of ulcerative colitic symptoms in 648 patients.

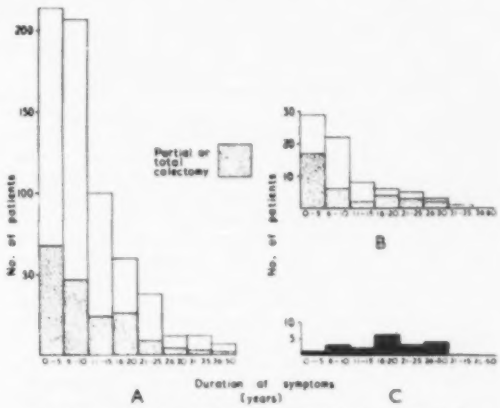
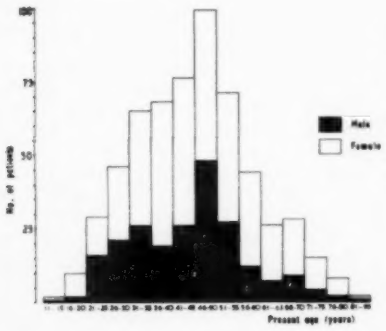
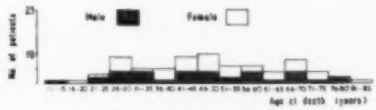


FIG. 127.—Analysis of 648 patients with ulcerative colitis according to duration of disease. A, Total number of patients studied; B, Number of patients deceased; C, Patients with carcinoma of the large bowel.





A B

FIG. 128.—Ages of ulcerative colitic patients at time of 1958 survey. A, Ages of 589 living patients in December, 1958; B, Ages of 74 deceased patients at time of death (1947–58).

Sex Incidence.—

Whole Group.—Four hundred and nine (61·7 per cent) of the patients were female, and 254 (38·3 per cent) were male, giving a ratio of 1·6 : 1.

Carcinoma Group.—Twelve (63·2 per cent) of these patients were female and 7 (36·8 per cent) were male, giving a ratio of 1·7 : 1.

Duration of Colitic Symptoms.—

Whole Group.—This is represented diagrammatically in *Fig.* 127 A, B. *Fig.* 127 A shows the findings for those patients where the age at onset was known (648 cases) in 5-year periods, and also shows the proportion of cases which have undergone large bowel resection at the Gordon Hospital. The average duration of colitic symptoms is 9·6 years (S.E.M. = 2·7); only 127 patients (19·6 per cent) are known to have had colitis for more than 15 years and only 227 (35·1 per cent) for more than 10 years. *Fig.* 127 B shows the duration of symptoms at the time of death in the 74 deceased patients; 12 of these died directly from carcinoma of the large bowel.

Carcinoma Group.—The duration of ulcerative colitic symptoms before the diagnosis of carcinoma was made is represented in *Fig.* 127 C. The average duration was 17·8 years (S.E.M. = 1·8) and 13 (68·5 per cent) of the 19 patients first experienced colitic symptoms more than 15 years prior to the discovery of carcinoma.

Age at Diagnosis of Carcinoma.—In the 19 patients developing large intestinal carcinoma the average age at diagnosis of cancer was 43·9 years (S.E.M. = 2·4); only 3 patients were over 55 years of age, 7 patients (36·8 per cent) were less than 40 years old, and the ages ranged from 24 to 63 years.

Age Distribution of the Whole Group of Ulcerative Colitis Patients.—Of the 589 patients still alive, the average age at the time of this survey (December, 1958) was 44·8 years (S.E.M. = 3·2) with 79 patients (13·4 per cent) over 60 years of age and 194 (33 per cent) over 50 years of age. The ages are given diagrammatically in *Fig.* 128 A for 5-year periods according to sex.

The age distribution of the 74 deceased patients (of whom 12 died as a result of large bowel cancer) is shown in *Fig.* 128 B. The average age at death was 47·7 years (S.E.M. = 4·4).

Presenting Clinical Features of Patients developing Carcinoma.—As can be appreciated

from the case histories there was no specific clinical picture indicating the presence of carcinoma in ulcerative colitis. Any or all of the symptoms described might have occurred in the natural course of the colitis without cancer. The presence of a stricture, however, does seem to be an important feature which should always raise the possibility of carcinoma.

Distribution and Severity of Colitis.—

Whole Group.—The distribution is given in *Table II*. The severity was estimated histologically in 284 cases. We consider that this is too small a proportion and the material too selective to give a representative histological picture for the whole group.

Carcinoma Group.—The distribution is given in *Table II* and the severity in *Table III*.

Macroscopic Features of the Carcinoma.—

Site.—In 10 cases the carcinoma was in the rectum or rectosigmoid region; in 7 cases, growths were present in the colon. In 4 of these 17 cases it was difficult to determine the precise site of the tumour macroscopically. In 2 cases the primary site was undetermined (*Cases* 18 and 19; *Table III*).

Presence of Stricture.—In 7 cases a stricture was diagnosed prior to operation for carcinoma. Whether this stricture preceded or was caused by the carcinoma is discussed below.

Spread and Metastasis.—In 12 cases the growth was widespread in the serosa and there was lymphatic involvement.

Multiplicity of Growth.—In only 1 case (*Case* 10) were two separate carcinomas present. In *Case* 18 the whole large bowel was diffusely involved by carcinoma but the precise site of origin was not determined.

Microscopic Features of the Carcinoma.—

Differentiation of Growth.—The growth was well differentiated in 4 cases, moderately differentiated in 6, and poorly differentiated (or anaplastic) in 7 (*see Table III*). In *Case* 19 only metastases were available for histology.

Mucus Secretion.—In 18 cases (*Case* 19 excluded) mucus secretion was marked in 4, moderate in 8, and absent in 6.

Peri-acinar Fibrous Stromal Reaction.—In 8 cases irregular isolated carcinomatous acini lying in the submucosa were surrounded by extensive deposits of fibrous tissue. We have not found this to be a conspicuous feature of carcinoma of the large intestine apart from that arising in ulcerative colitis; its possible significance is discussed below.

Presence of Polyps.—In the 17 cases where an adequate examination was possible we have found polyps indistinguishable from true neoplastic adenomas, and in relation to the carcinoma in 9 cases (*Table III*). There were pseudopolyps as previously defined in 6 cases. In these 6 cases polypoid lesions were present which had features of both true and pseudopolyps and in 3 of these cases these lesions appeared to have undergone malignant change. The possibility of transition from pseudopolyp to neoplastic polyp and carcinoma is discussed below.

Mortality.—

Whole Group.—*Table IV* summarizes the causes of death in 74 patients included in the ulcerative colitis follow-up series at the Gordon Hospital who died between 1947 and 1958. Twelve (16·2 per cent) of the deaths are directly attributable to large bowel carcinoma. Neoplastic disease, not of the large intestine, was the cause of death in 4 patients (including *Case* 1 discussed below).

Carcinoma Group.—Thirteen of the 19 patients are dead and all except one died as a result of large intestinal cancer. The exception was *Case* 1 whose death was caused by a retroperitoneal sarcoma 7 years after the removal of a colonic carcinoma. Nine patients died within a year of the discovery of carcinoma, and of the 6 patients alive in December, 1958, 5 had been followed-up for 12 months or less from the time of diagnosis of cancer of the large bowel.

Table IV.—Causes of Death in 74 Cases of Ulcerative Colitis (1947–58)

Cause of Death	No. of Cases	Percentage Total Deaths
Ulcerative colitis (no operation)	13	17·6
Ulcerative colitis (post-operative)	28	37·8
Carcinoma large bowel	12	16·2
Carcinoma elsewhere*	4	5·4
Miscellaneous causes not associated with carcinoma or ulcerative colitis	17	23·0

*Primary growth—gall-bladder, cervix, retroperitoneal sarcoma, stomach.

DISCUSSION

Age at Onset of Ulcerative Colitis.—The patients in the carcinoma group appeared to develop colitic symptoms at an earlier age when compared with the whole group of ulcerative colitic cases. Jackman, Bargen, and Helmholtz (1940) have suggested that ulcerative colitis in childhood is more likely to develop carcinomatous change than the disease beginning in adult life. However, we feel that the longer duration of disease in those cases starting in childhood is more important than the age of onset.

Sex.—The larger number of females in the carcinoma group is probably a reflection of the increased incidence of ulcerative colitis in females in the whole series. The sex distribution in the whole group of cases contrasts with the findings of Sloan, Bargen, and Gage (1950) who reported a female to male ratio of 0·8 : 1 in their series of 2000 patients.

Duration of Ulcerative Colitis.—The present findings are similar to the observations of most workers that large intestinal cancer tends to arise in patients with long-standing colitic lesions. It is therefore important to note that in the whole group of cases we have reviewed, only 19·6 per cent have suffered from their illness for more than fifteen years, thus indicating that our survey involves a group of patients whose disease is of relatively short duration and may therefore not show a maximum incidence of carcinomatous change in the bowel at the present time. It is interesting to note that of 127 patients with more than fifteen years' history of ulcerative colitis 13 developed carcinoma; this incidence of 10·2 per cent is almost four times the crude incidence for the whole series.

The present survey may therefore be too early to give significant statistical results and it will be necessary to review this work at intervals of five years or longer.

The long duration of colitic symptoms before carcinoma occurred has also been noted by Bargen and Sauer (1944), Counsell and Dukes (1952), Goldgraber and others (1958), and others. This aspect serves to emphasize the liability of carcinoma to develop in long-standing colitis and the need for special care in the follow-up of such cases, whether clinically active or quiescent.

Age at Diagnosis of Carcinoma.—The average age at discovery of large bowel cancer in the carcinoma group of patients is appreciably lower than the average age at diagnosis of large intestinal cancer in the general population. It has also been shown that the average age of the 663 colitic patients is below the usual age range for the development of large bowel cancer.

Distribution and Severity of Colitis.—There were 3 cases in the carcinoma group which were all distal or more extensive and were graded as indeterminate because a partial or total distribution could not be excluded. If these cases are considered as distal or partial colitis the distribution of ulcerative colitis in the carcinoma group is not greatly different from that in the group as a whole.

All cases in the carcinoma group were in the chronic active or quiescent phases. This corresponds to the findings of other workers (though Case 3 of Cattell and Boehme's 1947 series developed carcinoma in a fulminating colitis of only three months' duration), and is in keeping with the long-standing history of colitis prior to the development of carcinoma. Of the 6 cases in the quiescent group, 5 developed carcinoma of the rectum and only 1 a carcinoma of the colon.

Statistical Analysis.—We have attempted to estimate the importance of large intestinal carcinoma in ulcerative colitis by studying its occurrence in a large number of colitic patients. By this means we have obtained a 'crude incidence' of 2·9 per cent in the present series. Statistical evaluation of this figure is difficult because of the small number of cases involved, not all of which are of random occurrence. Seven of the 19 carcinoma cases were thought to have a large bowel cancer when they were first referred to the Gordon Hospital, and in 2 instances a surgical resection of the growth had been performed previously elsewhere. Another problem in a study of this type is the difficulty of maintaining an accurate follow-up of the whole group of patients. Twenty-two of the 663 patients have been untraced for more than one year and some of these have gone abroad. Although it is possible that the development of cancer may therefore be missed in such cases, no notification of the death of any of the untraced patients has been made to the Registrar General.

A further factor which is difficult to evaluate statistically in our series is the effect of large intestinal resection. We have received the whole or part of the colon from 183 patients and further operations have been performed elsewhere in other cases; in only 4 cases has the entire large bowel been removed. In the majority of patients treated surgically a total colectomy has been performed accompanied by an ileorectal anastomosis. Therefore, in more than 28 per cent of patients the length of bowel 'at risk' is very much reduced and the relative incidence of carcinoma may thereby be affected.

In addition to the special problems in this survey there are other factors which may influence the results of workers studying the incidence of carcinoma. Firstly, several series have consisted entirely of ulcerative colitis patients from whom the colon had been resected (e.g., Counsell and Dukes, 1952); such patients would form a specially selected group and a full pathological study of the bowel would be possible in every case. The incidence of carcinoma would be higher in such a survey and similarly the incidence would be higher in centres where the majority of patients are treated surgically. Secondly, in view of the difficulties in detecting the onset of cancer clinically, death may be attributed to the ulcerative colitis although malignant change has developed. It is therefore possible that the development of carcinoma may remain unrecognized if an autopsy is not performed.

However, despite the problems of assessing the incidence of carcinoma, statistical data have been of value in studying age factors and the duration of colitis. These results have been discussed above and have provided further evidence to support the clinical and pathological impressions that carcinoma develops in long-standing colitis and that it occurs at a relatively younger age than in the general population.

Macroscopic Features of the Carcinoma.—The relative distribution of the growth—10 rectal and 7 colonic carcinomas with 2 of undetermined site—is not greatly different from the usual distribution of large intestinal carcinoma. It also roughly

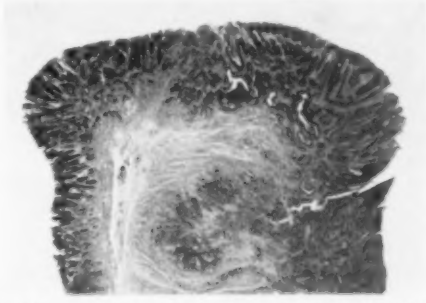


FIG. 129.—*Case* 13. Carcinoma of cæcum in colitis arising diffusely over a wide field. Note the lack of abrupt origin. Hæmatoxylin and eosin. (× 4.)

parallels the distribution of colitis, and it is probable that carcinomas are more prone to arise first in that part of the bowel which is involved earliest and most frequently in colitis.

In 3 cases where the growth was in the colon it was difficult even on close inspection of the resected bowel to determine the precise site of the carcinoma. In one patient (*Case* 18) the whole large intestine was diffusely involved by carcinoma and careful autopsy did not reveal the site of primary growth; in a further case (*Case* 19) the site of primary growth was not

determined at laparotomy. This lack of definition has been observed by other workers, e.g., Counsell and Dukes (1952), Goldgraber and others (1958), and may well be due to the fact that the growth frequently arises as a diffuse carcinomatous change over a wide field of mucosa, in sharp contrast to the usual large intestinal carcinoma where the edge of the growth is well defined (*Fig.* 129).

Early spread and metastasis is a feature of our series, as of others (Counsell and Dukes); it is linked with the poor prognosis to be discussed.

One of our patients (*Case* 10) developed two carcinomas, and one a diffuse carcinomatous involvement (*Case* 18); others were found to have a carcinoma in one site and adenomatous polyps elsewhere. Multiplicity of growths is common in most reported series (12 out of 41 cases reported by Sauer and Bargen, 1949; and 5 out of 14 cases described by Goldgraber and others, 1958), and our series is unusual in this respect.

FIG. 130.—*Case* 2. Stricture of colon in which a carcinoma had arisen. The ulcerative colitic lesion is clearly seen but the carcinomatous change cannot be made out with the naked eye.

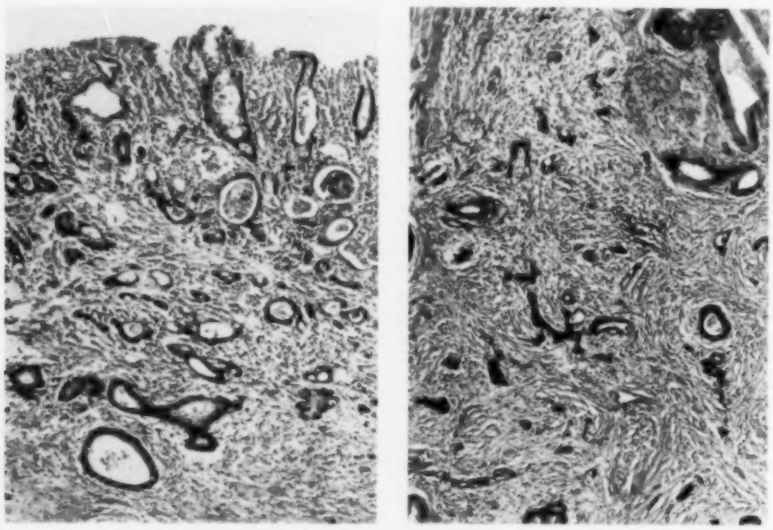


FIG. 131.—*Case* 10. Carcinomatous gland elements with peri-acinar fibrosis in the submucosa. A possible derivation from islands of buried epithelium (*see Fig.* 132) is suggested. Hæmatoxylin and eosin. (× 50.)

Seven cases out of 17 had strictures diagnosed at the time of discovery of carcinoma (*Fig.* 130). Three of the cases (*Cases* 9, 10, and 13) had developed these strictures more than a year before the diagnosis of carcinoma and in two others (*Cases* 6 and 19) the stricture probably preceded the growth. Counsell and Dukes also noted the frequent occurrence of strictures, but attributed them to the carcinoma; we feel that carcinomas sometimes arise at a preformed stricture and that the presence of a stricture requires a careful survey for carcinoma.

Microscopic Features of the Carcinoma.—The degree of differentiation of the growths and mucin-secreting activity are summarized in *Table III*.

In general, the rectal growths are more poorly differentiated and more actively mucus-secreting than those of the colon, and have arisen from areas where the ulcerative colitis is quiescent.

In 8 of the 17 growths available for histolog cal examination, isolated irregular gland acini lie in the submucosa or inner muscle-coat and are surrounded by dense fibrous tissue in which are varying numbers of chronic inflammatory cells (*Fig.* 131). They are clearly carcinomatous, for they are hyperplastic

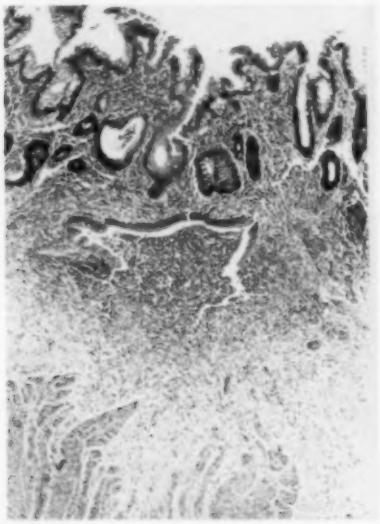


FIG. 132.—Island of buried epithelium in ulcerative colitis. Hæmatoxylin and eosin. (× 40.)

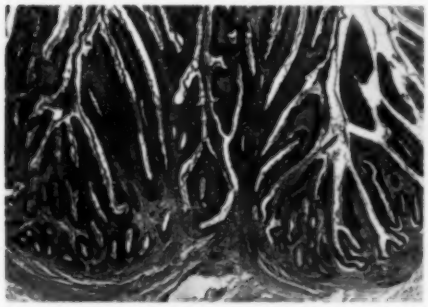


FIG. 133.—*Case* 13. Papilloma, apparently of characteristic neoplastic pattern, from a case of ulcerative colitis. Hæmatoxylin and eosin. (× 20.)

and invade the muscle-coats. Nevertheless, they are not unlike the irregular islands of 'buried' epithelium which are found in the submucosa in chronic active ulcerative colitis without carcinoma (*Fig.* 132) and they may in fact arise from such buried islands. In support of this hypothesis it is interesting to note that Warren and Sommers (1949), writing of ulcerative colitis, state: "regeneration of mucosal epithelium continues . . . and eventually foci of precancerous epithelial hyperplasia develop in the unfavourable environment." Such an origin for at least some of the carcinomas would explain their diffuseness and poor macroscopic definition.

A number of cases has been described in which there has been diffuse infiltration of submucosa, muscle-coats, and serosa of the colon by signet-ring cells with an associated fibrous stromal reaction, producing a 'leather bottle' colon similar to linitis plastica (Karstens and Bargen, 1947; Laufman and Saphir, 1951; Goldgraber and others, 1958). Secondary growth from carcinoma of the stomach must be excluded. We have not seen this appearance in any of our cases.

Relationship of Polyps to Carcinoma.—Many workers (Sauer and Bargen, 1949; Rose, 1947; Johnson and Orr, 1948; Goldgraber and others, 1958; and others) have remarked that polyps are often present in the region of carcinomas in ulcerative colitis, and we have found some form of polyp in 9 out of 17 cases. These have been variously described as pseudopolyps (Goldgraber and others), as true adenomatous polyps (Johnson and Orr), and there has been much discussion as to whether pseudopolyps can ever become true neoplastic polyps. Swinton and Warren (1939) and Counsell and Dukes (1952) describe the different types of polyp and believe with Hardy, Brooke, and Hawkins (1949) that the pseudopolyps of ulcerative colitis never become neoplastic; Warren and Sommers (1949) state: "inflammatory polyps . . . are considered least likely to undergo malignant change." Other workers take the opposite view. Yeomans (1927) writes: "the transition from simple inflammatory hyperplasia to tumours pathologically cancerous can be traced through the stages of inflammation, gland cell hypertrophy and hyperplasia and adenoma to definite adenocarcinoma." Bargen (1928) reached the same

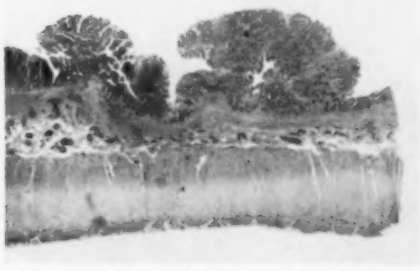


FIG. 134.—*Case* 10. Adenoma, apparently of characteristic neoplastic pattern, from a case of ulcerative colitis. Hæmatoxylin and eosin. (× 4.)

conclusion and cited other references; in subsequent publications (Brust and Bargen, 1934; Bargen and Sauer, 1944; Sauer and Bargen, 1949, etc.) he has strongly upheld his original views. He is supported by Goldgraber and others (1958).

Our own observations support those of Bargen. In 9 cases (*Table III*) we have found one or more polyps which are indistinguishable histologically from true neoplastic adenomas or papillomas (*Figs.* 133, 134). In 6 of these 9, pseudopolyps indistinguishable histologically from those commonly seen in ulcerative colitis without carcinoma are also present. In these 6 all forms of transitional lesion between true polyps and pseudopolyps can be seen.

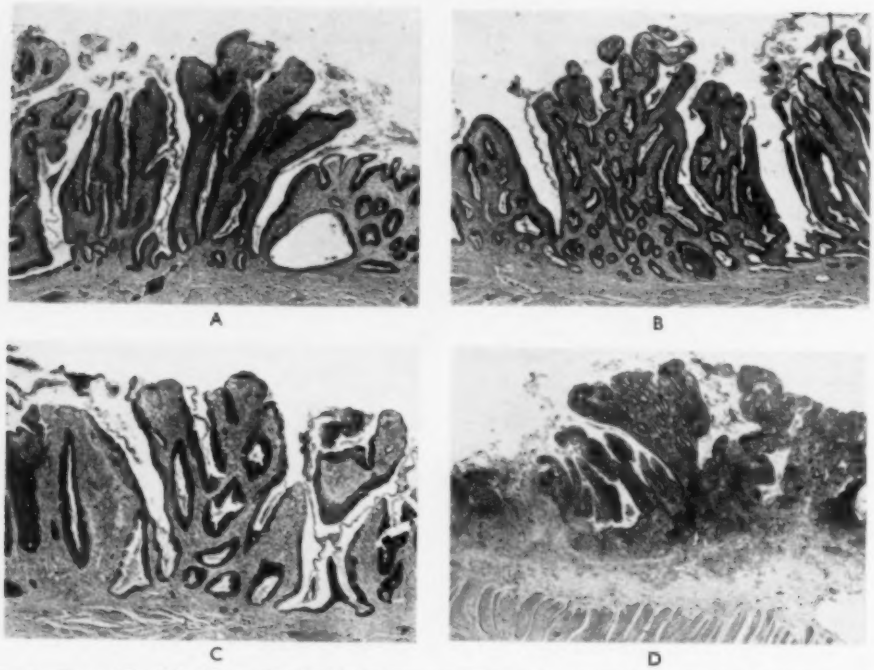


FIG. 135.—*Case* 13. Transitional forms of papillary lesion between papilloma of *Fig.* 133 and the pseudopolyp of D. Hæmatoxylin and eosin. (× 20.)

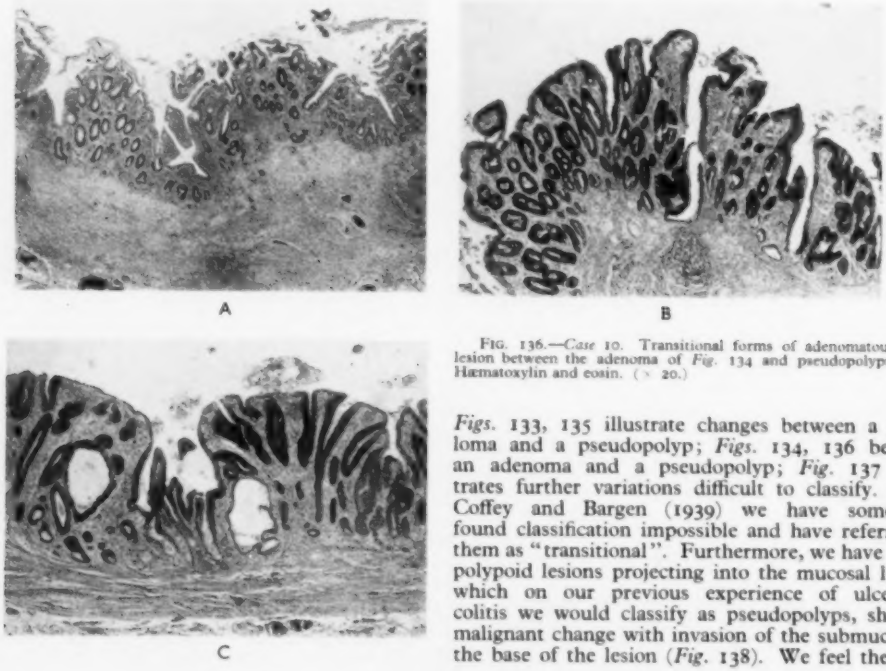
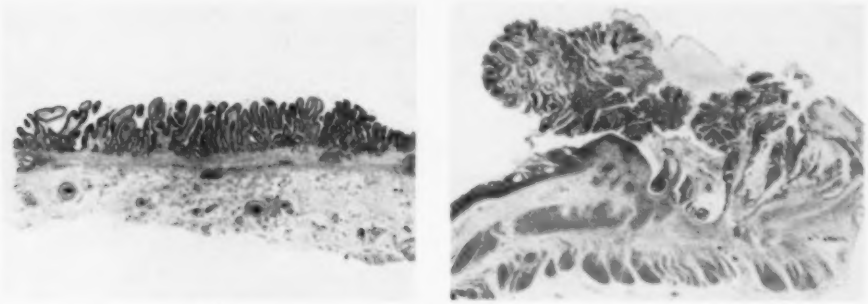


FIG. 136.—*Case* 10. Transitional forms of adenomatous lesion between the adenoma of *Fig.* 134 and pseudopolyps. Hæmatoxylin and eosin. (× 20.)

Figs. 133, 135 illustrate changes between a papilloma and a pseudopolyp; *Figs.* 134, 136 between an adenoma and a pseudopolyp; *Fig.* 137 illustrates further variations difficult to classify. With Coffey and Bargen (1939) we have sometimes found classification impossible and have referred to them as "transitional". Furthermore, we have found polypoid lesions projecting into the mucosal lumen, which on our previous experience of ulcerative colitis we would classify as pseudopolyps, showing malignant change with invasion of the submucosa at the base of the lesion (*Fig.* 138). We feel therefore

that pseudopolyps are capable of direct malignant transformation at their base to produce invasive adenocarcinoma, and that they are also capable of transformation to adenomatous and papillary lesions not readily distinguishable from true adenomas or papillomas, and like them, capable of malignant change.



A B

FIG. 137.—A, *Case* 5; B, *Case* 12. Further transitional forms of polypoidal papillary lesions. Hæmatoxylin and eosin. (× 4.)

Prognosis.—The prognosis of carcinoma in ulcerative colitis is unusually poor, mainly because there are no specific features to suggest its early diagnosis. Twelve of the present cases had local lymph-node involvement and 5 were inoperable when first investigated. These facts serve to emphasize the necessity for regular follow-up of the chronic case of ulcerative colitis, the potential importance of strictures, and any change in clinical features. We have not sufficient material to be satisfied that any of the pathological features we have described can be related to the prognosis.

The following are case histories of 19 patients with ulcerative colitis who developed carcinoma of the large bowel.

CASE REPORTS

Case 1.—

CLINICAL HISTORY.—

1938.—F. W., male, aged 35 years, had diarrhœa with blood and mucus which continued intermittently until 1951.

October, 1951.—Sigmoidoscopy. Rectal stricture at 10 cm. Admitted to the Gordon Hospital. Total colectomy was performed (Mr. H. G. Ungley) when carcinoma was incidentally discovered. The patient was then aged 47 years, and it was 13 years since the onset of colitic symptoms.

July, 1958.—Died from retroperitoneal sarcoma, aged 56 years, 21 years after the onset of ulcerative colitis and 7 years after removal of carcinoma.

PATHOLOGICAL EXAMINATION.—

1951.—Total colectomy. Bowel lumen narrowed throughout with absence of normal mucosal pattern.

Microscopically.—In one part there was polypoidal mucosal hyperplasia with irregular gland acini beginning to invade the muscularis mucosæ, interpreted as being early adenocarcinoma.

July, 1958.—Autopsy. Retroperitoneal sarcoma. There was no histological evidence of carcinoma.

SUMMARY.—Carcinoma of colon. Chronic active ulcerative colitis. Total distribution.

Case 2.—

CLINICAL HISTORY.—

1943.—Q. F., female, aged 20 years, developed diarrhœa with blood and mucus which continued intermittently until 1951.

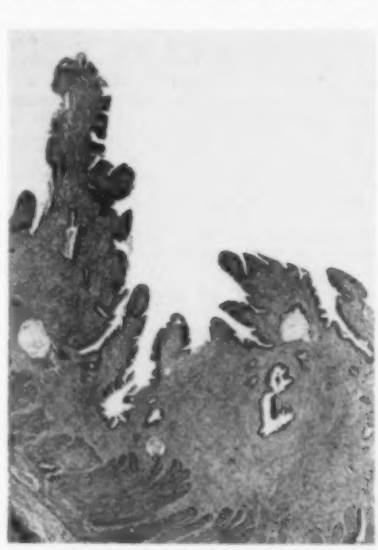


FIG. 138.—*Case* 6. Pseudopolyp undergoing malignant change at the base. Invasive carcinoma is present in adjacent fields. Hæmatoxylin and eosin. (× 15.)

1951.—Eight years after the onset of colitis, when aged 28 years, she developed increased frequency of stools containing blood and mucus, pain in the right side of her back, and fever. Clinical examination revealed a right pleural effusion, ascites, and a cystic mass in the pelvis. At laparotomy the small bowel was studded with multiple secondary deposits and there were bilateral ovarian tumours. The primary carcinoma of the colon was not recognized at that time. Bilateral salpingo-oöphorectomy and subtotal hysterectomy were performed.

October, 1951.—Died 12 days after operation.

PATHOLOGICAL EXAMINATION.—

September, 1951.—Uterus and cervix with both Fallopian tubes and ovaries resected. Both ovaries contained secondary carcinoma.

October, 1951.—Autopsy. The wall of the transverse colon was thickened over a distance of some 6 cm., and the lumen markedly narrowed (*Fig.* 130). At the site of thickening the colon was adherent to the greater curve of the stomach, but the stomach itself was free from growth throughout. Numerous small nodules of secondary growth were scattered throughout the peritoneal cavity.

Microscopically.—Very poorly differentiated mucus-secreting adenocarcinoma arising in the narrowed zone of transverse colon and infiltrating muscle-coats and serosa.

SUMMARY.—Carcinoma of colon. Chronic active ulcerative colitis. Total distribution.

Case 3.—

CLINICAL HISTORY.—

1925.—F. F., female, aged 37 years, had diarrhœa with blood and mucus which continued intermittently until 1950.

October, 1950.—Severe uterine hæmorrhage followed by an exacerbation of the diarrhœa with blood and mucus.

April, 1951.—Admitted to the Gordon Hospital. Mucus-secreting adenocarcinoma of rectum diagnosed. Laparotomy (Mr. S. O. Aylett) revealed metastatic deposits throughout the peritoneal cavity.

May, 1951.—Patient died, aged 63 years, 26 years after the first symptoms of ulcerative colitis.

PATHOLOGICAL EXAMINATION.—

May, 1951.—Autopsy. Anaplastic mucus-secreting adenocarcinoma of rectum breaching muscle-coats and extending into serosa. Numerous deposits of secondary carcinoma were present in the mesentery.

SUMMARY.—Carcinoma of rectum. Quiescent ulcerative colitis. Total distribution.

Case 4.—

CLINICAL HISTORY.—

1927.—F. E., female, aged 20 years, developed intermittent diarrhœa followed later by multiple para-anal fistulæ.

1938.—Surgical cure of the fistulæ attempted unsuccessfully elsewhere. Thereafter the area became a mass of granulation tissue on to which fistulous tracks opened periodically and discharged pus. Further treatment refused until 1952.

January, 1952.—Admitted to the Gordon Hospital with multiple fistulæ around the anus, and a mass palpable through the posterior vaginal wall. Abdominoperineal resection of the rectum with total hysterectomy, bilateral salpingo-oöphorectomy, and excision of the fistulæ (Mr. R. W. Raven) for rectal carcinoma invading the cervix uteri. The patient was then 45 years old and symptoms of ulcerative colitis had begun 25 years previously.

June, 1954.—Died from secondary carcinoma.

PATHOLOGICAL EXAMINATION.—

March, 1952.—Operation. Terminal 29 cm. of large intestine and anus resected with uterus, cervix, and part of vagina. A carcinoma of the rectum, with lower edge 4 cm. from the anus, involved 4 cm. of the rectum and infiltrated the uterus and cervix anteriorly. Polyps were present adjacent to growth.

Microscopically.—Moderately well differentiated mucus-secreting adenocarcinoma. At one edge irregular gland elements penetrated muscle-coats. They were surrounded by fibrous tissue suggesting a possible origin from buried epithelium.

June, 1954.—Autopsy. Secondary adenocarcinoma in the pelvis.

SUMMARY.—Carcinoma of rectum. Quiescent ulcerative colitis. Total distribution.

Case 5.—

CLINICAL HISTORY.—

1950.—D. D., female, aged 29 years, developed diarrhœa with blood and mucus which continued intermittently until 1957.

February, 1957.—Re-admitted to Gordon Hospital. Barium enema showed a stricture of the rectosigmoid region and sigmoidoscopy and rectal biopsy revealed carcinoma. Abdominoperineal resection of the rectum with removal of the uterus and appendages was performed (Mr. S. O. Aylett). She was then aged 36 years and had been suffering from ulcerative colitis for 7 years.

September, 1957.—Deteriorated and died from secondary carcinoma.

PATHOLOGICAL EXAMINATION.—

February, 1957.—Operation. Terminal 37 cm. of large intestine and anus removed with the uterus, both Fallopian tubes, and ovaries. An extensive carcinoma arose diffusely over 12 cm. of the rectum with its lower edge 6 cm. from the anorectal junction. Pseudopolyps, true polyps, and transitional forms (*Fig.* 137 A) present elsewhere in the bowel but not in the region of carcinoma.

Microscopically.—Poorly differentiated mucus-secreting adenocarcinoma infiltrating muscle-coats and serosa.

September, 1957.—Autopsy. Generalized carcinomatosis.

SUMMARY.—Carcinoma of rectum. Chronic active ulcerative colitis. Partial distribution.

Case 6.—

CLINICAL HISTORY.—

1935.—A. D., male, aged 18 years, developed intermittent diarrhœa until 1941.

1946.—Began to experience increasing difficulty in defæcation over the next 6 years.

May, 1954.—Sigmoidoscopy revealed two fibrous strictures of the rectum, one 10 cm. from the anus; the second, which biopsy showed to consist of adenocarcinoma, 20 cm. from anus. The patient was then 37 years old and symptoms of ulcerative colitis had first occurred 19 years previously.

June, 1954.—15 cm. of colon resected. A carcinoma obstructed the lumen. Numerous small nodules were seen in the peritoneum.

February, 1955.—Developed intestinal obstruction, was treated elsewhere, and died.

PATHOLOGICAL EXAMINATION.—

June, 1954.—Operation. 15 cm. of colon resected. The lumen at the distal resected end was almost completely blocked by a large cauliflower-like tumour. The mucosa immediately proximal had a nodular appearance. The remainder of the bowel appeared healthy.

Microscopically.—Well differentiated adenocarcinoma arising in an area of chronic active ulcerative colitis. In places there were masses which histologically were pseudopolyps undergoing malignant change (*Fig.* 138); elsewhere the appearances were more suggestive of adenomatous polyps. Transitional stages between the two types were present. Irregular isolated gland elements surrounded by fibrous tissue lay in the submucosa and muscle-coats. Appearances suggested an origin from islands of 'buried' epithelium often present in active ulcerative colitis.

February, 1955.—Autopsy. Well differentiated mucus-secreting adenocarcinoma was found above and below the line of anastomosis, which was itself intact.

SUMMARY.—Carcinoma of colon. Chronic active ulcerative colitis. Distribution indeterminate (certainly distal, possibly total).

Case 7.—

CLINICAL HISTORY.—

1952.—E. A., male aged 49 years, developed diarrhœa with blood continuing for 2 years.

August, 1954.—Rectal hæmorrhage investigated elsewhere. Double diagnosis of ulcerative colitis with a possible carcinoma of the transverse colon suggested.

October, 1954.—Admitted to Gordon Hospital for total colectomy and ileorectal anastomosis (Mr. S. O. Aylett). The patient was then aged 51 years and colitic

symptoms had begun 2 years before. Post-operative recovery was satisfactory.

October, 1958.—Remained well when last seen 4 years after colectomy.

PATHOLOGICAL EXAMINATION.—

October, 1954.—Operation. Terminal 9 cm. of ileum, cæcum, appendix, and approximately 75 cm. of large intestine resected. A large carcinoma involved some 8 cm. of the transverse colon, infiltrating the muscle-coats and constricting the lumen. The adjacent mucosa appeared polypoid. Metastases in adjacent lymph-nodes.

Microscopically.—Rather poorly differentiated mucus-secreting adenocarcinoma arising diffusely over a wide field of mucosa and infiltrating muscle-coats. Local lymph-nodes contained deposits of secondary growth. The adjacent mucosa had a polypoidal pattern, which had features both of an adenomatous polyposis and pseudopolyposis with intermediate changes.

SUMMARY.—Carcinoma of colon. Chronic active ulcerative colitis. Total colitis.

Case 8.—

CLINICAL HISTORY.—

1935.—R. P., female, aged 12 years, developed diarrhœa with blood and mucus, treated surgically elsewhere, probably by appendicostomy.

1954.—Complained of anal discomfort and abdominal distension accompanied by constipation and later by diarrhœa.

December, 1954.—Anterior resection of rectum and right ovary performed at the Gordon Hospital (Mr. S. O. Aylett). The patient was then 31 years old and symptoms of ulcerative colitis had begun 19 years previously.

April, 1955.—Remaining large bowel resected for colitis. Ileorectal anastomosis performed. Condition deteriorated and patient died some weeks later. No autopsy performed.

PATHOLOGICAL EXAMINATION.—

December, 1954.—Operation. 20 cm. of sigmoid colon and rectum resected. In the upper rectum a papillary tumour arose from the mucosa over a length of 5 cm. and projected into the lumen. The bowel was narrowed at this point.

Microscopically.—Papillary adenocarcinoma suggesting malignant transformation of a papilloma and providing no evidence of origin from pseudopolyps. Dilated gland elements surrounded by fibrous tissue were present in submucosa and muscle-coats and suggested a possible origin from 'buried' epithelium.

April, 1955.—Operation. Terminal 7 cm. of ileum, cæcum, and appendix and 60 cm. of colon removed. No evidence of carcinoma.

SUMMARY.—Carcinoma of rectum. Chronic active ulcerative colitis. Total distribution.

Case 9.—

CLINICAL HISTORY.—

1933.—S. C., female, aged 21 years, developed recurrent diarrhœa with blood and mucus.

1939.—Left iliac colostomy performed elsewhere because of the development of a rectal stricture.

1942.—Barium-enema radiograph showed narrowing and shortening of the whole of the large bowel.

December, 1942.—Terminal ileostomy and appendicectomy performed elsewhere (Mr. A. L. Abel).

September, 1949.—Colon excised (Mr. A. L. Abel) for ulcerative colitis leaving a non-functioning rectum and lower sigmoid colon behind.

July, 1951.—Rectum perforated necessitating surgical repair. Ileorectal anastomosis no longer possible.

September, 1956.—Twenty-three years after the onset of colitis, and when aged 45 years, the patient was admitted to the Gordon Hospital. Laparotomy revealed an inoperable tumour involving the rectum and anal canal with peritoneal deposits of growth. Died 10 days after the operation.

PATHOLOGICAL EXAMINATION.—

1949.—Operation. Specimen consisted of the cæcum and 26 cm. of large intestine. No carcinoma present.

October, 1956.—Autopsy. Distal sigmoid colon and rectum markedly thickened and narrowed by a carcinoma arising diffusely and spreading outwards to involve surrounding tissues.

Microscopically. Anaplastic mucus-secreting adenocarcinoma arising from a rectal stump.

SUMMARY.—Carcinoma of rectal stump. Chronic active ulcerative colitis at operation in 1949. Total distribution.

Case 10.—

CLINICAL HISTORY.—

1937.—D. M., female, aged 30 years, developed sudden onset of diarrhœa with blood and mucus which continued until 1947, after which she had a remission till 1952.

1952.—Developed a rectal stricture which needed dilatation on four occasions.

October, 1956.—A barium-enema radiograph showed a narrowing of the ascending colon as well as a rectal stricture.

March, 1957.—Admitted to the Gordon Hospital where total colectomy was performed (Mr. S. O. Aylett) with ileorectal anastomosis. Two areas of carcinoma found in colon. The patient was then aged 50 years and ulcerative colitis had been present for 20 years.

September, 1958.—Died from secondary carcinoma.

PATHOLOGICAL EXAMINATION.—

March, 1957.—Operation. Terminal 9 cm. of ileum, cæcum, and 63 cm. of large intestine resected. A constricting carcinoma of the ascending colon 8 cm. from the ileocæcal valve partly occluded the lumen over a distance of 3 cm. Polyps were present just distal to this growth. A second separate constricting carcinoma involved the descending colon over a distance of 3 cm. just distal to the splenic flexure.

Microscopically.—The tumour in the ascending colon consisted of isolated irregular but moderately well differentiated gland elements in the submucosa, muscle-coats, and serosa, surrounded and separated by fibrous tissue (*Fig.* 131). The growth in the descending colon had a similar pattern in the superficial submucosa, but in the deeper submucosa and muscle-coats it was much more anaplastic with mucus-secretion, and peri-acinar fibrosis was not a feature. One polyp appeared to be a true benign adenomatous polyp (*Fig.* 134), but intermediate forms were present (*Fig.* 136).

SUMMARY.—Two carcinomas of colon. Quiescent ulcerative colitis. Total distribution.

Case 11.—

CLINICAL HISTORY.—

1934.—S. W., female, aged 28 years, developed diarrhœa which continued intermittently with blood and mucus until 1958.

March, 1958.—Total colectomy performed (Mr. A. L. Abel) with ileorectal anastomosis for colitis. An unsuspected adenocarcinoma of the colon was discovered. The patient was then aged 52 years and symptoms of ulcerative colitis had begun 24 years previously.

December, 1958.—Laparotomy to remove fistulous track. No evidence of carcinoma.

PATHOLOGICAL EXAMINATION.—

March, 1958.—Operation. Terminal 18 cm. of ileum, cæcum, and 95 cm. of colon. At the distal end was a small sessile polypoid area not macroscopically carcinoma.

Microscopically.—The polypoid area described was a poorly differentiated adenocarcinoma forming large gland elements with some surrounding fibrosis. It was invading muscle-coats but had not yet breached them. Appearances did not suggest an origin from pseudopolyps.

SUMMARY.—Carcinoma of colon. Chronic active ulcerative colitis. Total distribution.

Case 12.—

CLINICAL HISTORY.—

1930.—G. A., female, aged 31 years, developed diarrhœa. Symptoms improved temporarily during pregnancy but recurred over the next 4 years, following which she remained well for 11 years.

1946.—Recurrence of loose stools containing blood and mucus intermittently until 1958.

1958.—Diarrhœa became severe and more frequent and she began to have a sensation of incomplete defæcation; later she became increasingly constipated.

August, 1958.—Admitted to the Gordon Hospital, after diagnosis of rectal carcinoma, for abdominoperineal excision of the rectum (Mr. A. L. Abel). This patient was then aged 59 years and the onset of ulcerative colitis had occurred 28 years before.

November, 1958.—Well.

PATHOLOGICAL EXAMINATION.—

August, 1958.—Operation. Terminal 29 cm. of large intestine and anus resected. A large raised growth 8 cm. long partly surrounded the lumen of the lowest part of the rectum; the bowel above appeared atrophic.

Microscopically.—Moderately well differentiated mucus-secreting adenocarcinoma with a predominantly papillary pattern which had invaded muscle-coats but had not breached them nor involved the serosa or adjacent lymph-nodes. It appeared in places to have arisen from a pre-existing papilloma, in places from a pseudopolyp, and intermediate changes were present.

SUMMARY.—Carcinoma of rectum. Chronic active ulcerative colitis. Distribution indeterminate (certainly distal, possibly total).

Case 13.—

CLINICAL HISTORY.—

1939.—A. T., female, aged 39 years, developed intermittent diarrhœa with passage of blood.

June, 1958.—Attended the Gordon Hospital because of severe rectal bleeding. A large rectal polyp was considered doubtfully malignant after biopsy on two occasions. Barium enema showed severe colitis with stricture formation.

September, 1958.—Total colectomy performed (Mr. R. W. Raven) with ileorectal anastomosis. Strictures and polypoid areas were noted at operation. The patient was then aged 57 years and symptoms of ulcerative colitis had begun 19 years before.

November, 1958.—Well.

PATHOLOGICAL EXAMINATION.—

1958.—Operation. 17 cm. of ileum, cæcum, and appendix, and 84 cm. of large intestine resected. Marked thickening of ileocæcal valve, due to carcinoma arising from the mucosa over the valve and encircling the base of the appendix. Distal to the hepatic flexure the bowel wall was thickened and pseudopolyps were present. At the splenic flexure and at the distal resected end of the specimen there were areas where sessile papillary projections resembling true papillomas arose from the mucosa.

Microscopically.—The ileocæcal valve was largely replaced by a moderately well differentiated adenocarcinoma arising from the covering mucosa and infiltrating muscle-coats. The usual abrupt origin was lacking (*Fig*. 129). Polypoid tumours were present also at hepatic and splenic flexures and in the descending and sigmoid colon. They projected into the ileum as broad adenomatous papillary structures without a central core of connective tissue, but with numerous crypt abscesses and much stromal inflammatory change. They appeared to represent a transition from pseudopolyps to true papillary adenomas (*Figs*. 133, 135).

SUMMARY.—Carcinoma of cæcum. Active chronic ulcerative colitis. Total distribution.

Case 14.—

CLINICAL HISTORY.—

1938.—J. M., male, aged 4 years, developed intermittent diarrhœa for 4 years, after which remission occurred until the age of 17 years.

1952.—Diarrhœa recurred and was accompanied by blood.

August, 1955.—Total colectomy performed (Mr. S. O. Aylett) with ileorectal anastomosis for colitis. The patient made a satisfactory recovery with clinical improvement.

September, 1958.—Re-admitted to the Gordon Hospital with sacral pain. Adenocarcinoma infiltrating anus confirmed by biopsy. Abdominoperineal excision of the rectum performed (Mr. S. O. Aylett) for a large growth of the anorectal region infiltrating the pararectal tissues, prostate, posterior urethra, and bladder base. At the time of diagnosis of rectal carcinoma this patient was 24 years old and had suffered from ulcerative colitis for 20 years.

PATHOLOGICAL EXAMINATION.—

1955.—Operation. Terminal 6 cm. of ileum, cæcum, and 58 cm. of large intestine resected. No evidence of carcinoma.

September, 1958.—Operation. Ileorectal anastomosis excised with rectum and anus. A large carcinoma with raised, rolled edges occupied the distal 6 cm. of rectum infiltrating beneath the anal skin, and causing marked rectal stenosis. The growth had breached the muscle-coats and invaded adjacent lymph-nodes.

Microscopically.—Moderately well differentiated mucus-secreting adenocarcinoma in which isolated neoplastic gland elements tended to be surrounded by fibrous tissue.

SUMMARY.—Carcinoma of rectum below ileorectal anastomosis. Chronic active ulcerative colitis 1955, quiescent 1958. Total distribution.

Case 15.—

CLINICAL HISTORY.—

1937.—D. M., female, aged 15 years, developed intermittent diarrhœa with blood lasting until 1947. She was then symptom-free till 1956.

September, 1956.—Noticed the passage of blood per rectum and increasing constipation.

November, 1956.—Ulcerating carcinoma found in the ampulla of the rectum which was firmly attached to surrounding structures. Abdominoperineal resection of the rectum and total hysterectomy performed elsewhere (Mr. R. W. Raven). At the time of operation this patient was 34 years old and symptoms of ulcerative colitis had begun 19 years before, remaining clinically inactive for the last 10 years.

August, 1957.—Ileotransverse colostomy to relieve intestinal obstruction due to a recurrence of growth in the pelvis.

November, 1957.—Died. Autopsy not performed.

PATHOLOGICAL EXAMINATION.—

November, 1956.—Terminal 33 cm. of large intestine, anus, uterus, and part of vagina resected. The rectum was encircled by a carcinoma involving 7 cm., the lower edge of the growth being 4 cm. from the anorectal junction. Numerous small mucosal tags were present above the growth.

Microscopically.—Poorly differentiated mucus-secreting adenocarcinoma.

SUMMARY.—Carcinoma of rectum. Quiescent ulcerative colitis. Partial distribution.

Case 16.—

CLINICAL HISTORY.—

1938.—H. M., male, aged 29 years, developed intermittent diarrhœa with blood and mucus persisting till 1958.

January, 1958.—Following an exacerbation of diarrhœa and rectal bleeding, he was found to have a rectal carcinoma. He was then 49 years old and had been suffering from ulcerative colitis for 20 years. Abdominoperineal excision of rectum performed elsewhere. No secondary spread of growth seen at operation. Recovered well.

December, 1958.—Progress satisfactory.

PATHOLOGICAL EXAMINATION.—

January, 1958.—Part of pelvic colon, rectum, and anus resected. Plaque of growth with indefinite margins present 5 cm. above the anal margin.

Microscopically.—Well differentiated adenocarcinoma with an ill-defined margin invading muscle-coats. Individual gland elements are surrounded by fibrous tissue.

SUMMARY.—Carcinoma of rectum. Quiescent ulcerative colitis. Distribution indeterminate (certainly distal, possibly total).

Case 17.—

CLINICAL HISTORY.—

1931.—C. B., male, aged 18 years, developed diarrhœa which continued intermittently for 25 years.

May, 1956.—Admitted elsewhere following the discovery of a rectal growth infiltrating sacral tissues, which was excised together with the colon distal to the colostomy (Mr. H. G. Ungley). Patient was then aged 45 years and symptoms of ulcerative colitis had begun 27 years before.

June, 1958.—Died at home. No autopsy.

PATHOLOGICAL EXAMINATION.—

June, 1957.—Rectum, anus, and a length of colon resected. Fungating carcinoma present in rectum.

Microscopically.—Anaplastic adenocarcinoma which invaded the serosa but was not mucus secreting.

SUMMARY.—Carcinoma of rectum. Ulcerative colitis not histologically confirmed. Distal distribution.

Case 18.—

CLINICAL HISTORY.—

1951.—G. L., male, aged 28 years, developed abdominal pain and backache followed by severe intermittent diarrhœa.

April, 1956.—Transferred to the Gordon Hospital. Laparotomy (Mr. S. O. Aylett) revealed extensive growth throughout the peritoneal cavity with hepatic metastases. The patient died 10 days later at the age of 33 years, having suffered from ulcerative colitis for 5 years.

PATHOLOGICAL EXAMINATION.—

April, 1956.—Autopsy. Greater omentum and peritoneum widely infiltrated by secondary growth. No primary tumour found in any organ after very careful search.

Microscopically.—Serosal surface of the bowel, omentum, and liver infiltrated by poorly differentiated adenocarcinoma with an appearance consistent with a primary origin in the large intestine. Sections of bowel did not reveal a primary growth, but in view of the negative results of careful search elsewhere, a diffuse origin from large intestinal mucosa is probable.

SUMMARY.—Carcinoma, primary site undetermined. Active chronic ulcerative colitis. Total distribution.

Case 19.—

CLINICAL HISTORY.—

1944.—M. W., female, aged 33 years, developed persistent diarrhœa with periods of incomplete remission and exacerbation.

1956.—Rectal stricture detected.

August, 1958.—Developed lower abdominal pain radiating to the back; abdomen became swollen.

October, 1958.—Re-admitted to the Gordon Hospital. Laparotomy (Mr. S. O. Aylett) revealed ascites and tumour deposits in the liver. No primary growth identified in the alimentary tract or elsewhere, but in view of the metastases in the liver colectomy was not performed. The patient was then aged 47 years and had been suffering from ulcerative colitis for 14 years.

January, 1959.—Died. No autopsy.

PATHOLOGICAL EXAMINATION.—

1954, 1956, 1957.—Biopsies. Active chronic ulcerative colitis with pseudopolyps.

October, 1958.—Biopsy. Metastasis in liver from a poorly differentiated mucus-secreting adenocarcinoma. Appearances were consistent with a primary carcinoma of the large intestine, but primary growth in another organ, e.g., stomach, could not be excluded histologically.

SUMMARY.—Carcinoma, primary site undetermined. Active, chronic ulcerative colitis. Total distribution.

SUMMARY AND CONCLUSIONS

1. A consecutive series of 663 patients suffering from ulcerative colitis, attending the Gordon Hospital during the eleven and three-quarter years ending December, 1958, has been studied. Nineteen cases of large intestinal carcinoma were found, giving a crude incidence of 2·9 per cent. Full details of the criteria adopted in this study are given and the case reports are presented.

2. The results for the whole group of patients and the group which developed carcinoma are analysed in terms of age at onset of colitis, sex, duration of colitic symptoms, age at time of survey or at diagnosis of carcinoma, distribution and severity of colitis, macroscopic and microscopic features of cancer, the presence of polypoid lesions, and cause of death.

3. The development of carcinoma appears to be related to the duration of colitis rather than to the age at onset. The average age at diagnosis of cancer was younger than the usual age for cancer of the large bowel. Difficulties in the statistical evaluation of results are discussed.

4. Macroscopically, the growth was sometimes difficult to define. Strictures were sometimes associated with carcinoma and are discussed. Early spread beyond the bowel and early metastasis were common features. Carcinoma in the colon developed on a basis of chronic active ulcerative colitis, while carcinoma of the rectum developed in active or quiescent colitis.

5. Microscopic features of the carcinoma are discussed and the possible origin from 'buried' epithelium considered.

6. Polyps were frequently associated with the carcinoma. They were of adenomatous, pseudopolypoid, and transitional forms. The possibility of transition from pseudopolyp to true adenoma and carcinoma is discussed.

7. The prognosis of carcinoma in ulcerative colitis is poor. Cases of ulcerative colitis, both chronic active and quiescent, of long duration, require careful, regular follow-up, with biopsy if possible, especially in the presence of stricture formation.

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REFERENCES

BARGEN, J. A. (1928), *Arch. Surg., Chicago*, **17**, 561.
— — and SAUER, W. G. (1944), *Clinics*, **3**, 516.
BRUST, J. C. M., and BARGEN, J. A. (1934), *New Engl. J. Med.*, **210**, 692.
CATTELL, R. B., and BOEHME, E. J. (1947), *Gastroenterology*, **8**, 695.
COFFEY, R. J., and BARGEN, J. A. (1939), *Surg. Gynec. Obstet.*, **69**, 136.
COUNSELL, B. P., and DUKES, C. E. (1952), *Brit. J. Surg.*, **39**, 485.
CROHN, B. B., and ROSENBERG, H. (1925), *Amer. J. med. Sci.*, **170**, 220.
FELSEN, J., and WOLARSKY, W. (1949), *Arch. intern. Med.*, **84**, 293.
GOLDGRABER, M. B., HUMPHREYS, E. M., KIRSNER, J. B., and PALMER, W. L. (1958), *Gastroenterology*, **34**, 809.
HARDY, T. L., BROOKE, B. N., and HAWKINS, C. F. (1949), *Lancet*, **2**, 5.
JACKMAN, R. J., BARGEN, J. A., and HELMHOLTZ, H. F. (1940), *Amer. J. Dis. Child.*, **59**, 459.
JOHNSON, T. M., and ORR, T. G. (1948), *Amer. J. dig. Dis.*, **15**, 21.
KARSTENS, H. C., and BARGEN, J. A. (1947), *Proc. Mayo. Clin.*, **22**, 231.
LAUFMAN, H., and SAPHIR, O. (1951), *Arch. Surg., Chicago*, **62**, 79.
LUMB, G., and PROTHEROE, R. H. B. (1958), *Gastroenterology*, **34**, 381.
ROSE, W. McI. (1947), *J. Path. Bact.*, **59**, 483.
SAUER, W. G., and BARGEN, J. A. (1949), *J. Amer. med. Ass.*, **141**, 982.
SLOAN, W. P., BARGEN, J. A., and GAGE, R. P. (1950), *Gastroenterology*, **16**, 25.
SWINTON, N. W., and WARREN, S. (1939), *J. Amer. med. Ass.*, **113**, 1927.
WARREN, S., and SOMMERS, S. C. (1949), *Amer. J. Path.*, **25**, 657.
WHEELOCK, F. C., and WARREN, R. (1955), *New Engl. J. Med.*, **252**, 421.
YEOMANS, F. C. (1927), *J. Amer. med. Ass.*, **89**, 852.

A STUDY OF PANCREATOGRAPHY

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INTRODUCTION

THE elective performance of pancreatography during the course of abdominal exploration upon subjects with pancreatic disease is being increasingly used. The present study was undertaken in order to correlate the radiological appearances of the duct system of the pancreas with the histological findings in patients without overt pancreatic disease. The intention has been to provide a basis for the interpretation of operative pancreatograms obtained in the living subject, and to investigate the incidence of epithelial metaplasia and hyperplasia in routine necropsy material.

METHOD OF INVESTIGATION

The material was obtained at routine necropsy at St. Bartholomew's Hospital from adult subjects dying from a wide variety of acute and chronic disease. Apart from the exclusion of cases of known primary pancreatic disease, an attempt has been made to examine an unselected series of organs from consecutive patients. A few specimens have been excluded in which obvious post-mortem autolysis made investigation valueless. A total of 150 pancreases have been studied.

The series consisted of 94 male subjects and 56 females; in the males, age at death ranged from 24 to 81 years (average 56·6) and in the females from 28 to 84 years (average 58·6).

The pancreas was removed from the body intact, together with the duodenal loop. The duodenum was opened and a probe passed down into it through the common bile-duct to locate the papilla. The latter was then lifted away from the duodenal wall with a pair of toothed dissecting forceps and the duodenal mucosa was dissected back as a cuff until about 1 cm. of the wall of the ampulla was exposed. By making a small nick in the inferior aspect of the ampulla the main pancreatic duct could be easily entered. A 2-mm. blunt-ended cannula was tied into the duct and radio-opaque medium was injected by means of a 10-ml. syringe. In the first 105 specimens the radio-opaque medium was bismuth oxychloride in gelatin, prepared to the London Hospital formula. The mass was injected after warming to 60° C. and solidified on cooling within about one minute. Although no difference was apparent in the quality of the pancreatograms, the large particle size of this medium was found to obscure somewhat the subsequent histological examination. For this reason a standard microcrystalline stable suspension of barium sulphate (micropaque) was used in the final 45 specimens and gave much better results. It remained within the duct system in a satisfactory manner and had the added advantages of improved storage, the possibility of injection at room temperature, and good histological appearances. The suspension was used without dilution. The injection was made slowly and gently until a slight sense of resistance could be felt, and was also controlled by watching the injected mass run distally along the main pancreatic duct, beneath the surface of the pancreas; in some cases medium could be seen escaping from the lesser pancreatic duct. An average volume of 2 ml. was required to fill the ducts, but there was some variation in the amount necessary. In a small proportion of specimens injection by the above route was unsuccessful, but was achieved either by cannulation of a prominent lesser duodenal papilla or by retrograde injection along the main duct after transection of the tip of the tail of the pancreas. Injection by one of

these methods was successful in 150 organs; a further 6 specimens were rejected because of a technically unsatisfactory injection.

All radiographs were made immediately, using a portable X-ray machine in the necropsy room. An exposure of 15 mA. sec. at 60 kV. was used and the film was standard clinical X-ray film, without intensifying screens.

After radiography, the organs were placed at once in 5 per cent formol saline for fixation and were re-examined after scrutiny of the films. The best results were obtained after about 24 hours' fixation. The material was sliced with the knife at about 0·5 cm. intervals and examined for gross abnormality, after which an average of 4 histological sections were made from each pancreas, varying between 2 and 10 sections. A standard hæmatoxylin and eosin staining technique was used, but van Gieson's and mucicarmine stains also were employed when necessary.

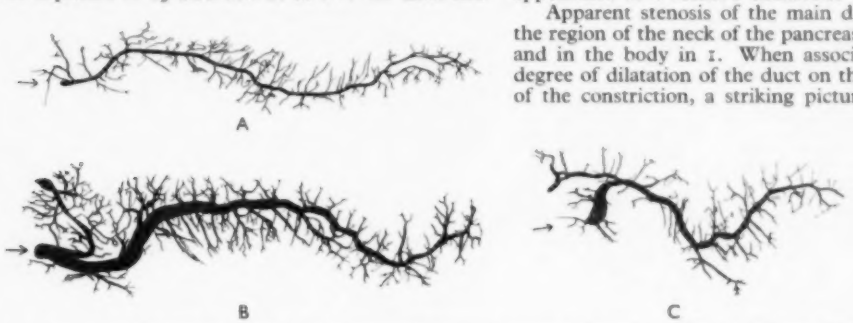


FIG. 139.—Variations in calibre of main pancreatic duct. A, Maximum diameter 2·0 mm. B, Maximum diameter 8·3 mm. C, Maximum diameter 7·2 mm. Terminal dilatation of main duct. Arrow indicates site of injection. (× $\frac{1}{10}$.)

RADIOLOGICAL FINDINGS

Main Pancreatic Duct.—Examination of the pancreatograms revealed some diversity in the appearance of the major pancreatic ducts. The length of the main duct naturally varied with the size and shape of the organ, but striking differences in the calibre of this channel were encountered. The radiographs were made with the specimens in direct contact with the X-ray film, so that the magnification error could be neglected.

The diameter of the main pancreatic duct at its widest part was recorded after direct measurement from the pancreatograms. These maximum diameters varied between 1·8 and 9·2 mm., having an average of 4·1 mm. (*Fig.* 139). The widest part of the main duct was in the head of the pancreas in the majority of organs, but localized enlargement in the body was sometimes seen. The region of the sphincter of the main duct was not often visible, owing to the technique of injection, but this segment was usually a narrow one, so that the 3–5 cm. of the main duct traversing the head presented the appearance of a relative dilatation.

Apparent stenosis of the main duct was seen in the region of the neck of the pancreas in 7 specimens and in the body in 1. When associated with some degree of dilatation of the duct on the duodenal side of the constriction, a striking picture was obtained (*Fig.* 140). In only 2 of the specimens with apparent ductal stenosis did subsequent histological examination reveal that the lesion was produced by pathological change, in both cases metastatic carcinomatous infiltration. In the remaining 6 specimens with a narrow zone, histological examination showed that the appearance was produced either by a mucosal fold or by narrowing at the point where the main pancreatic duct, passing through the neck of the pancreas, passed on to a more ventral plane to enter the head of the gland. There was frequently a pronounced S-shaped segment of the duct at this site (*see Fig.* 145). The sections failed to show pathological change in the wall of the duct in any of these examples. The histology also appeared normal in the specimens showing terminal dilatation of the main duct, as well as those—representing about 10 per cent of the series—in which the duct had an undulating fusiform outline (*Fig.* 141), a pancreatographic appearance due to anatomical folding of the wall of the duct, without any associated abnormality in the surrounding parenchyma.

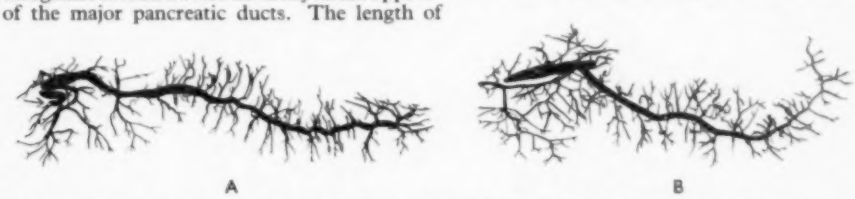


FIG. 140.—Apparent stenosis of main duct. A, Due to mucosal fold in head sector. B, Due to angulation of main duct at neck of pancreas.

Accessory Pancreatic Duct.—This channel was visible in the pancreatograms in 102 organs, representing 68 per cent of the series. It could not be seen in 41 specimens (27·3 per cent). Finally, in a total of 7 organs (4·7 per cent) the main channel of the pancreas emerged from the so-called accessory papilla, which in these cases was a misnomer. As a general rule, no attempt was made to cannulate both

the duodenal orifices of the pancreatic ducts; consequently the figure of 68 per cent represents an approximate minimal incidence of the accessory ductal system since, apart from one case in which the two systems were injected separately, the method used did not demonstrate the accessory ductal system in the organs in which it had no communication with the main duct.

In 19 specimens, although an accessory duct could be seen on the pancreatograms, duodenal efflux did not occur during the injection of the medium; the accessory duct was patent in the remaining 83 specimens in which it filled (55·3 per cent of the total series). The nature of the apparent obstruction of the orifice of the accessory duct was not fully investigated. It may have been due in some examples to post-mortem contraction of the smooth muscle surrounding its orifice. However, irregular penetration of the medium in the terminal part of the accessory duct (*Fig.* 142) was a common appearance in the series, and was associated with a histological finding of partial blockage of this region with an inspissated material resembling dental tartar, and in a few cases by hyperplastic ductal epithelium.

It was not possible to investigate the incidence of a 'common channel' for bile and pancreatic secretions, owing to the method of injection, but much has been published on this subject (Rienhoff and Pickrell, 1945).

FIG. 141.—Variations in outline of main pancreatic duct. A, Dilatation and irregularity of middle sector. B, Irregularity of whole length. Note large duct from inferior part of head.

Secondary Pancreatic Ducts.—The pancreatograms confirmed the finding of Cordier and Arsac (1952) that in those specimens in which the main pancreatic duct traverses the upper part of the head of the pancreas a very large secondary duct drains a wide territory in the lower part of the head. This duct, described by Cordier as "*le canal inférieur de la tête du pancréas*", is frequently nearly as wide as the main duct. It joins the lower aspect of the main pancreatic duct (*Fig.* 141 B).

In addition to expected variations in number, length, and calibre, appearances of obvious dilatation, irregularity of outline, or cyst formation were seen in the secondary ducts in 15 specimens (10 per cent), while a further 41 (27·3 per cent) showed minor irregularity or beading of scattered ducts. The site of these lesions was not limited to any particular region in the pancreas, but was most common in the secondary ducts of the head and often affected widely scattered ducts, those in the intervening regions appearing entirely normal (*Fig.* 142). The most frequent appearances were fusiform or saccular dilatation, but secondary ducts looking like a string of spherical beads were occasionally seen (*Fig.* 143). The irregularities were present in all degrees of

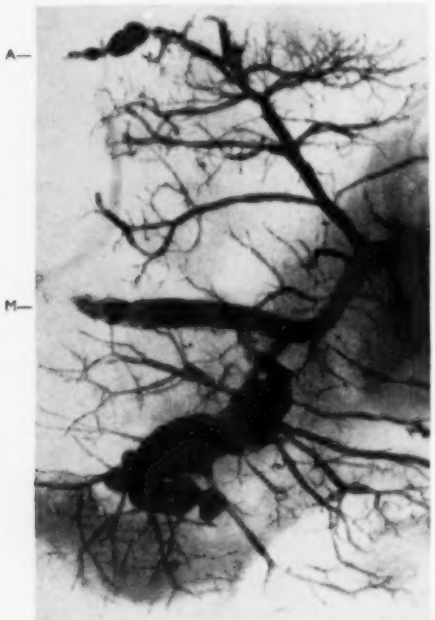


FIG. 142.—Irregular filling of accessory duct and pancreatectasis of an isolated secondary duct. The accessory duct A showed intraductal epithelial hyperplasia and accumulation of inspissated secretion. M, Main pancreatic duct. (× 1·6.)

FIG. 143.—Moniliform dilatation of isolated secondary duct in middle sector, associated with localized intraductal and glandular hyperplasia. (× 1·6.)

severity, varying from isolated beading or irregularity in a few isolated ducts to a widespread saccular development of large tracts of the secondary ductal system, to which it seems justifiable to refer to as *pancreatectasis* (*Figs.* 144, 145).

Incomplete filling of the secondary ducts was noted in 15 organs (10 per cent). Occasionally the appearance may have been due to imperfect penetration of the medium; however, in most cases the injection was evenly distributed throughout the ductal system, and the subsequent histology revealed that poor filling was the result of blockage of the minor ducts with inspissated mucinous material (*Fig.* 146).

Owing to the wide variation in the topography of the secondary ductal system, 'silent areas' could not

FIG. 144.—Irregular dilatation of isolated secondary duct. Neighbouring ducts unaffected. (× 1·6.)

be distinguished in any of the pancreatograms, in spite of the fact that a number of small space-occupying lesions, generally due to metastatic tumour deposits, were encountered on sectioning the material.

Artefacts.—Opacities due to acinar filling or local extravasation of the medium were seen in 23 specimens in the series (15·3 per cent). They occurred either when the pancreas had undergone post-mortem autolysis, in which case diffuse acinar filling was the result, or when too much force had been used during the injection. Acinar filling produced a fine, diffuse haze throughout the parenchyma, often partially obscuring the ductal pattern. Local extravasations were of two principal types—small, fairly regular, multiple disk-like opacities, and irregular local extravasations, usually single. The localized artefacts could be easily identified as a rule by the small size of the opacities and by the relative freedom of the pancreas in these specimens from abnormalities of the secondary ducts. However, in two instances a radiological appearance of an irregular opacity was thought to represent an isolated extravasation, but subsequent microscopical examination showed that it was due to filling of a pseudocyst in a pathological area of pancreatic necrosis.

Localized artefacts were not found in the presence of acinar filling, since it appears that once a small duct had ruptured, any increase in the volume of the injection invariably resulted in further extravasation into the same area.

FIG. 145.—Pancreatectasis in multiple secondary ducts in head of pancreas. Tortuosity of main pancreatic duct is a normal variant. Histology showed mucous glandular hyperplasia around dilated ducts, which contained hyperplastic epithelium. (× 1·6.)

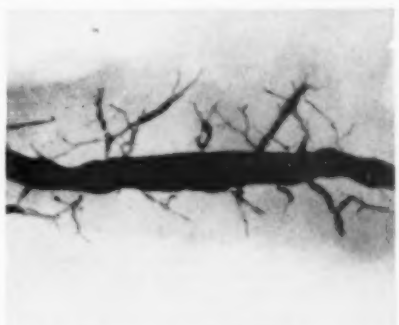
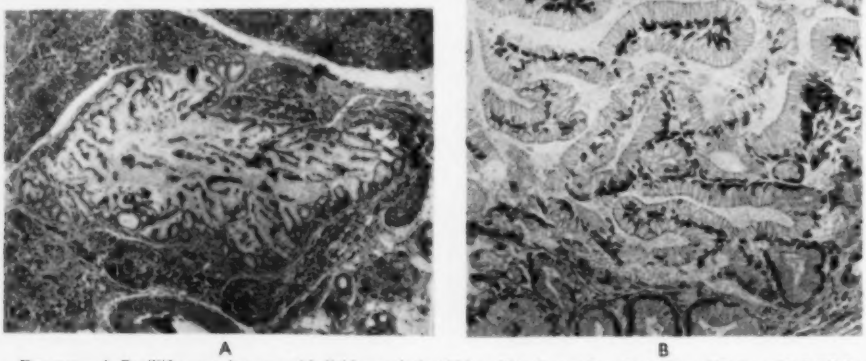


FIG. 146.—Stumpy appearance of secondary ducts due to poor filling in a specimen in which the ducts showed widespread obstruction by inspissated mucinous material. (× 1·6.)

HISTOLOGICAL FINDINGS

Columnar Epithelial Hyperplasia.—The most significant histological finding in the examination of the material from the 150 specimens in this investigation relates to the discovery of hyperplastic changes in the lining epithelium of the pancreatic ducts and

their associated mucous glands in 44 organs, an incidence in the series of 29·3 per cent. When the hyperplasia affected the columnar epithelium of the ducts, it took two common forms. The most striking appearance was a papilliferous intraductal proliferation of a mucus-secreting type of cell of extremely regular appearance. The resulting complete filling of the duct by this epithelium somewhat resembled a papilliferous adenoma (*Fig.* 147). The other



A B

FIG. 147.—A, Papilliferous columnar epithelial hyperplasia within a dilated secondary duct. H. and E. (× 16.) B, High-power view. Note mucus-secreting type of epithelium within the duct and in related hyperplastic intramural glands (below). H. and E. (× 100.)

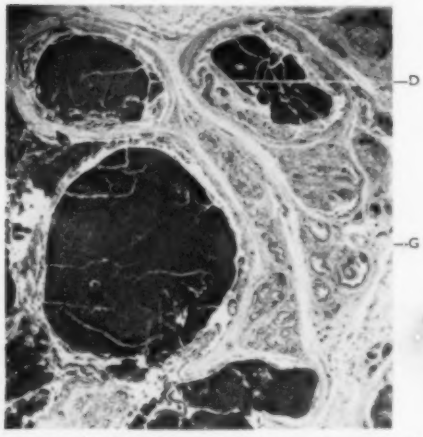


FIG. 148.—Section of several dilated spaces in a region of pancreatectasis. They contain radio-opaque medium. Note cushion-like proliferation of epithelium of duct, D, and area of glandular hyperplasia, G. *See also Fig.* 151. H. and E. (× 20.)

appearance, often less localized than the first type, consisted of cushion-like proliferation of the ductal epithelium (*Fig.* 148); it was often associated with the presence of squamous metaplasia elsewhere in the same organ.

Hyperplasia involving the mucus-secreting glands around the pancreatic ducts was encountered in 19 specimens, nearly all of which were also the seat of intraductal proliferation. The figure represents only those organs in which glandular development appeared very marked, and must be considered an approximation, since prominent intramural glands were seen in several other specimens which have been excluded. For this reason, it was difficult to establish an exact incidence of a true hyperplasia of these glands, which have a very wide range of development in the pancreas. Some difficulty was also experienced in a few examples in determining whether epithelial proliferations were arising in small ducts or within mucous glands related to larger ducts. All 19 examples classified as glandular hyperplasia showed penetration of the full thickness of the wall of the ducts by irregular glandular crypts lined with a tall columnar epithelium of mucus-secreting type. These cells showed a pale vacuolated cytoplasm and darkly staining basal-lying nucleus; in some specimens goblet cells were common, giving an appearance not unlike the epithelium of the colon. In several organs glandular overgrowth was very marked and the glands could be seen in the sections, lying outside the fibrous wall of the secondary ducts in the loose interlobular connective tissue, where they were often completely filled by hyperplastic mucus-secreting epithelium and desquamated cells. This type of periductal glandular proliferation was often associated with the formation of cystic spaces in close relation to the pancreatic ducts, with which they usually communicated. Most of these cysts appeared to represent grossly dilated secondary ducts rather than glandular structures, but in a few cases the glands themselves appeared to be dilated (*Figs.* 149, 150). The association of these cystic formations with radiological variations in the topography of the smaller pancreatic ducts will be discussed below.

Tables I and *II* show the incidence of the principal epithelial changes encountered, although in view of the focal pattern of these lesions it is probable that the actual incidence of hyperplastic epithelial change is higher than that suggested by the examination of an average of 4 random sections from each specimen. The site of the epithelial proliferation was the lining of the ducts in 39 specimens and their related mucous glands in 19. The general distribution of

the hyperplasia was similar whether the change involved the ducts or their glands, and had its greatest incidence in the secondary ducts and around the ampulla of the accessory pancreatic duct; it was seldom seen in the intramural glands of the main duct, although these glands are commonest in this situation. However, the ampullary region of the main duct, in which intramural glands occur frequently, was generally destroyed during the process of cannulation and therefore was not examined histologically. The low incidence of the change in the main pancreatic duct is only partially explained by the frequency with which its epithelium is found to have desquamated in necropsy material. The ampullary region of the accessory pancreatic duct, however, was a common site for the occurrence of the hyperplasia, often to an extreme degree, and frequently associated with an accumulation of inspissated secretion within the duct. Apart from this region, the proliferation showed in general a scattered distribution throughout secondary ducts and their larger tributaries in different parts of the pancreas, although in a few organs the majority of these ducts appeared to be involved. The ducts in the head of the pancreas were affected more frequently than those in other parts of the organ.

Table I.—INCIDENCE OF EPITHELIAL CHANGES RELATED TO PANCREATIC DUCTS (150 ORGANS)

	Number of Organs showing Changes	*Per cent*
Hyperplastic columnar epithelium	44	29·4
Metaplastic squamous epithelium	12	8·0

Table II.—TYPE OF EPITHELIAL CHANGE (150 ORGANS)

	Number of Organs showing Changes	*Per cent*
Columnar epithelium:		
Hyperplastic columnar epithelium in ducts	39	26·0
Hyperplastic columnar epithelium in glands	19	12·7
Squamous epithelium:		
Metaplastic squamous epithelium in ducts associated with columnar hyperplasia	9	6·0
Metaplastic squamous epithelium in ducts without columnar hyperplasia	3	2·0
Squamous epithelium within cysts	4	2·7

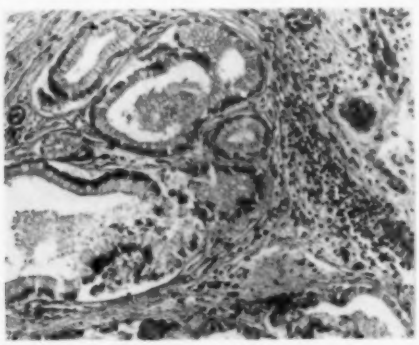


FIG. 149.—Scanty infiltration of chronic inflammatory cells around hyperplastic periductal mucous glands. Same specimen as *Fig.* 148. H. and E. (× 108.)

Columnar epithelial hyperplasia was encountered in 22 specimens from each sex. In the male examples, the age at death varied from 40 to 81 years (average 62) and in the females from 32 to 84 years (average 65).

Squamous Metaplasia.—In the total series, squamous epithelium was found in the pancreatic ducts in 12 organs, an incidence of 8·0 per cent. In a further four examples, squamous epithelium was found lining small isolated cysts. The distribution of the metaplasia in the ducts was similar to that seen in columnar hyperplastic change and principally involved the secondary and finer ducts. Metaplasia was not seen within the major channels, but was occasionally encountered within the intramural glands of the smaller ducts (*Fig.* 150). There was some variation in the appearance of the metaplastic epithelium, but it generally showed between two and five layers of cells, and prickle cells or keratinization were not seen. The lesions were very much less common than those due to columnar hyperplasia, since in many of the specimens in which metaplasia was recorded it was localized to only one or two isolated ducts. Moreover, the change was found to be a peculiarly patchy one, so that it frequently involved very short segments of the minor ductal system, in which it took the form of localized plaques and cushion-like formations (*Figs.* 151, 152). In a few other cases concentric metaplasia of very small ducts was seen (*Fig.* 153), but complete blockage of the ducts by squamous metaplasia appeared to be uncommon.

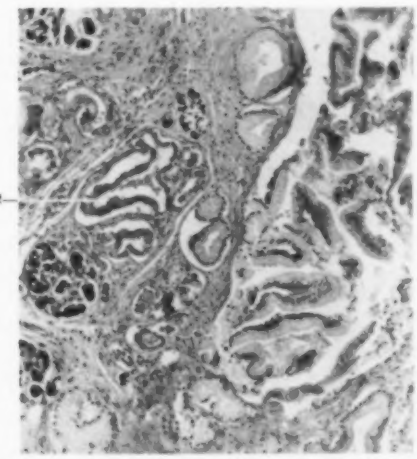


FIG. 150.—Early squamous metaplasia, M, within dilated glandular crypt related to a secondary duct which shows well-marked epithelial proliferation. H. and E. (× 68.)

Squamous metaplasia was nearly always found in association with columnar hyperplasia in the same pancreas (*see Figs.* 148, 151); the former change was seen in the absence of hyperplasia in only 3 examples and the two conditions coexisted in the remaining 9.

Inflammatory Lesions.—Focal areas of fat necrosis, combined in the more severe examples with patchy parenchymal necrosis, were seen in the sections from five organs. These lesions were never

widespread, but were very obvious in two of the specimens. The distribution of the necrotic areas was predominantly in the interlobular fatty connective tissue, but the adipose tissue around the pancreas was involved in one organ. In most instances, focal fat necrosis was unaccompanied by obvious cellular reaction, although some infiltration by small round cells was often present around the periphery of the lesions; the two more severely involved specimens showed diffuse polymorphonuclear infiltration of the areas of necrosis.

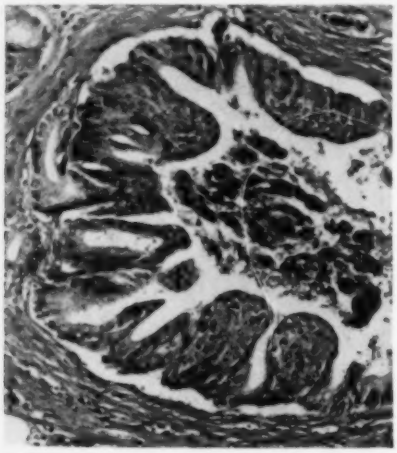


FIG. 151.—Cushion-like squamous metaplasia of epithelium lining a secondary duct. Same specimen as *Fig.* 148. H. and E. (× 124.)

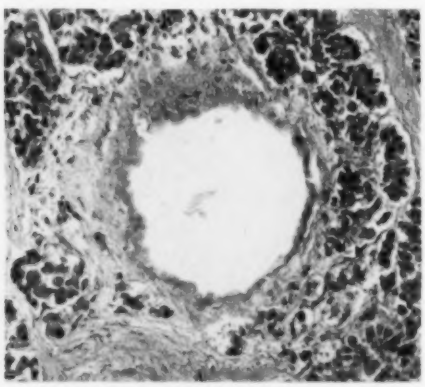


FIG. 153.—Squamous metaplasia within a small intralobular duct. H. and E. (× 124.)

Fat necrosis was not seen in any pancreas in which hyperplastic epithelial lesions were absent. In most instances it was not possible to trace any direct continuity between the necroses and the epithelial lesions; however, in two sections areas of necrosis were found in close proximity to abnormal glandular proliferation with cyst formation, and appeared to have arisen in relation to these (*Fig.* 154).

Apart from the cellular infiltration found in association with areas of pancreatic necrosis, inflammatory change was uncommon in the material studied. Scanty periductal collections of lymphocytes were occasionally seen, generally around regions in which

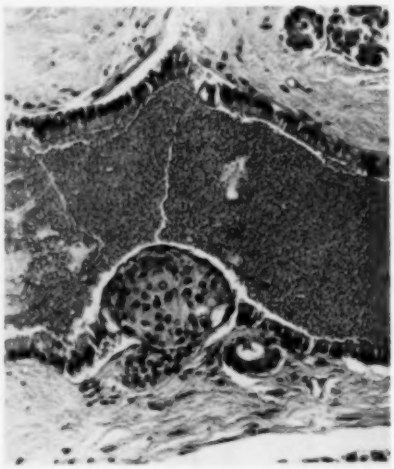


FIG. 152.—Nodule of squamous metaplasia within epithelium of otherwise normal secondary duct, which has completely filled with the medium. H. and E. (× 124.)

columnar epithelial proliferation was marked (*see Fig.* 149). Purulent exudate within the lumen of ducts was seen in only one specimen, which was one of those showing a more severe degree of patchy pancreatic necrosis in which the exudate also had a focal distribution.

Ductal Obstruction.—Localized areas of periacinar and perilobular fibrosis were seen in a few pancreases, sometimes accompanied by proliferation of very fine ductal elements, but these changes were invariably scanty. In most cases the fibrosis was apparently due to blockage of small ducts by intraductal epithelial proliferation or by a peculiar inspissated mucinous material which was often found within the ducts. Although often associated with epithelial overgrowth, this substance was sometimes seen in the presence of apparently normal epithelium. Replacement fibrosis due to ductal blockage by squamous metaplasia and widespread histological effects of ductal obstruction, such as are seen in lesions of the larger ducts, were not encountered.

Islet-cell Adenoma.—Two examples of islet-cell adenoma were discovered in the histological study of the specimens. They were both first noticed in the gross slices of the fresh pancreas, looking like very small lymph-nodes, one measuring 4 mm. and the other 6 mm. in diameter. The sections revealed the typical appearance of islet adenomata, well demarcated from the surrounding acinar tissue by a thin fibrous capsule. Both patients had died at the age of 66 years from unrelated causes and it seems unlikely that either of these small tumours had any endocrine function. The smaller of the adenomata occurred in a pancreas showing fairly widespread

areas of focal fat necrosis and intraductal and glandular epithelial hyperplasia. The other pancreas appeared histologically normal.

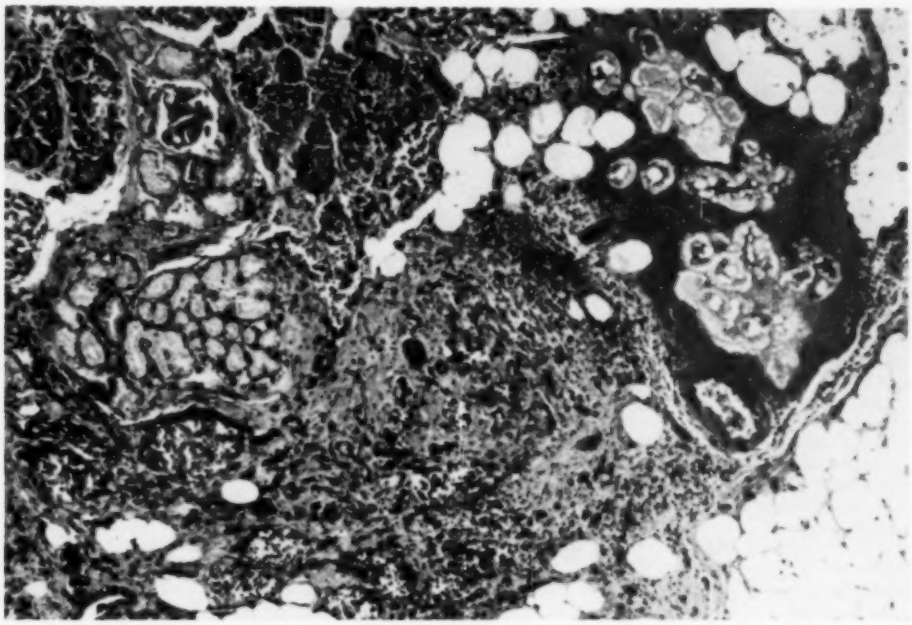


FIG. 154.—Subclinical interlobular fat necrosis. Area of necrosis (right) is separated from a hyperplastic epithelial lesion (left) by a zone of interstitial œdema and inflammatory reaction. H. and E. (× 34.)

DISCUSSION

During recent years it has been shown that valuable information can be obtained by the injection of radio-opaque medium into the main duct of the pancreas, and this procedure—operative pancreatography—has become established in the investigation of pancreatic disease requiring surgical treatment. The most frequent method has been the injection of a small volume of 70 per cent diodone through a fine polythene tube inserted into the duct of Wirsung after duodenotomy. In a few cases, adequate filling of the pancreatic ducts by reflux has been obtained during operative cholangiography, without recourse to direct exposure of the duodenal papilla (Leriche, 1930). These techniques have proved useful in localizing the site of a ductal obstruction in examples of pancreatic pseudocyst, and have demonstrated the wide range of appearances encountered in the ducts in patients suffering from chronic relapsing pancreatitis (Leger and Bréhant, 1956; Doubilet, Poppel, and Mulholland, 1957). Nevertheless, knowledge of variations in the normal and pathological anatomy of the pancreatic ductal system needs to be established by preliminary study of post-mortem material before the method can be expected to provide useful information in the living subject, and published accounts of abnormal radiographic appearances in patients with suspected pancreatic disease have not always been substantiated by morbid anatomical data. One reason for publishing the results of the present radiological and histological study of 150 pancreatic specimens has been to provide a basis for the interpretation of operative pancreatograms. The investigation has revealed unusual changes in the configuration of the secondary ducts in a significant proportion of subjects dying from unrelated causes. These appearances have been commonly found to be associated with structural changes in the ductal epithelium which have received insufficient recognition in the past.

Pancreatographic Appearances (*Figs.* 139–146).—A number of excellent studies of the radiological anatomy of the pancreatic ducts are already available (Reinhoff and Pickrell, 1945; Cordier and Arsac, 1952) and the present series adds little information concerning their configuration. However, considerable variation in the calibre of the main pancreatic duct was encountered, a finding of importance because it was apparently unassociated with any morbid anatomical abnormality. Diameters greater than 6 mm. were recorded in the main duct in 10 per cent of the specimens, in the largest of which it measured 9·2 mm., and the conclusion is reached that in the interpretation of pancreatograms a duct having a diameter less than that of an ordinary lead pencil (8 mm.) should not be considered wider than normal without additional evidence.

Fusiform dilatation of the terminal part of the main pancreatic duct was a common normal variant, as was apparent stenosis of the duct at the level of the neck of the pancreas. Newman, Weinberg, Newman, and Northup (1958), in a radiological study of the distal portions of the pancreatic and common

bile-ducts in 57 cadavers, encountered 5 instances of "an unusual dilatation of the major pancreatic duct" associated with "slight chronic pancreatitis" on microscopy in 3 of these. Six diagrams of main pancreatic ducts showing terminal widening are reproduced in their paper and are attributed to chronic pancreatitis, but differ in no respect from the appearance found in the present series in the absence of histological abnormality. Leger and Bréhant (1956) have described pancreatographic findings at operation in patients with chronic pancreatitis and have drawn attention to an appearance of "*sténose isthmique*", in which the main duct on either side of the narrow zone distends normally with the injected medium. Another radiographic picture reported by Leger and Bréhant as an occasional finding in cases of chronic pancreatitis has been a rigid irregular appearance of the slightly dilated pancreatic duct, with mild undulation of the outline. The present study reveals that both these variations in pancreatographic appearance of the main duct may be found without any related histological abnormality in the pancreas. The incidence of anatomical stenosis of the main pancreatic duct at the level of the neck in normal subjects has been found to be about 3 per cent, while an irregular wavy outline to the duct is found in about 10 per cent of subjects.

The pancreatograms revealed apparent abnormality in the outline of the minor pancreatic ducts in 10 per cent of the specimens, while in a further 27 per cent these showed lesser degrees of irregularity. Confining study to the fifteen organs in which obvious dilatation or cyst formation was visible in these ducts on the radiographs, subsequent histological examination revealed hyperplastic columnar epithelial change in the secondary ducts in 13, or 87 per cent. Of the two cases in which epithelial hyperplasia was not seen, one showed pancreatectasis to a marked degree although epithelium was unrecognizable, owing to autolysis; only two sections were examined from the other patient. In the examination of the histological material from the total series, dilatation of minor ducts and cyst formation was seen in 21 specimens and was associated with the presence of columnar epithelial hyperplasia in 18 of these (86 per cent). It is therefore apparent that radiological demonstration of dilatation and irregularity of the minor ducts reflects to an accurate degree the incidence of structural changes produced in these ducts by proliferation of the epithelium. This association is further supported by comparing the overall incidence of radiological irregularities in the minor ducts of 37 per cent with the figure of 29 per cent, representing the total incidence of epithelial hyperplasia. The difference between these proportions is readily explained by the fact that random histological sectioning was used, a technique unlikely to reveal the total incidence of a pathological change having a characteristically focal distribution.

Incomplete filling of secondary ducts was noted in 10 per cent of the pancreatograms and generally appeared to be due to blockage by inspissated mucinous material, usually in organs in which columnar hyperplasia was a feature. Poor filling of these ducts was not encountered in the twelve specimens which showed squamous metaplasia, as might be expected in view of the finding that the latter change seldom affected many ducts. However, specimens in which squamous epithelium was found almost always revealed evidence of the more widely distributed columnar epithelial proliferation in other parts of the organ. Consequently it seems probable that epithelial hyperplasia, with its associated changes of ductal dilatation and cyst formation, will be shown to be of greater importance in the production of surgical lesions in the pancreas than the less common and sparsely scattered areas of squamous metaplasia.

Morbid Anatomical Findings (*Figs.* 147–154).—The examination of the large amount of pancreatic material occasioned by the present study revealed certain chance findings, most of which are outside the scope of the present article. This applies to lesions such as hyperplasia of the islet tissue and diffuse acinar dilatation, a condition which probably reflects the functional state of the pancreatic secretory mechanism at the time of death, rather than any specific pathological condition (Stein and Powers, 1956). However, the somewhat unexpected finding of two examples of what appear to have been functionless islet-cell adenomata deserves record, since it confirms previous reports of the occurrence of sporadic clinically silent adenomata in the pancreas. Korpássy (1938) discovered four such lesions during an investigation of material from 500 pancreases from routine necropsy and his paper refers to other descriptions.

Since proliferation of columnar epithelium of the ducts and related glands was encountered in 29 per cent of the specimens, it is necessary to conclude that such a condition represents a normal histological variant in material from the age-group investigated. This conclusion accords with that of Yotuyanagi (1936 a), who carried out a very detailed histological study of the pancreas from 50 normal subjects in Japan. He encountered epithelial metaplasia in 64 per cent of his specimens, a proportion which seems unusually high, until it is noted that he used serial histological sectioning and also included in his total figure examples of what are now considered to be columnar epithelial hyperplasia. Yotuyanagi's Type-II metaplasia, which he found in 22 per cent of his specimens, corresponds to the columnar epithelial proliferation encountered in 29 per cent of the present series. The Japanese paper appears to contain the only previous published description of papillary and adenomatous types of ductal proliferation in normal material, but makes no reference to the striking alterations in the structure of the secondary ducts which, in the present study, frequently accompanied these epithelial variants. However, Wainwright (1951) observed cystic dilatation of small ducts; he attributed it to ductal obstruction by squamous metaplasia of the epithelium.

In specimens in which hyperplastic columnar epithelial hyperplasia was pronounced the secondary ducts, in which these lesions had their main incidence, were nearly always found to show dilatation and irregularity. The degree to which these were affected varied from a slight degree of irregular dilatation of isolated secondary ducts, revealed in the pancreatograms as fusiform or moniliform opacities (*see Figs.* 142–144), to a widespread development of multiple thin-walled cysts (pancreatectasis) (*see Fig.*

145). It was not always possible to determine whether these cystic structures arose from dilatation of the ducts themselves or in dilated glandular formations lying outside the wall of the parent duct with which they retained communication. In most examples, however, the saccular enlargements appeared to arise in expanded tortuous secondary ducts, the lining epithelium of which was invariably hyperplastic, with a variable degree of cushion-like or papillary proliferation (*see Fig.* 147). The mucous glands surrounding the dilatations usually appeared hypertrophied and frequently showed hyperplastic or metaplastic changes in their epithelium (*see Fig.* 150). In some examples these glandular structures showed similar cyst-like dilatation, although this could generally be distinguished from that affecting the ducts by the extreme thinness of their fibrous walls.

The various lesions described in relation to the secondary pancreatic ducts produced easily recognizable changes in the outline of the minor ducts in the pancreatograms, and the characteristic beaded appearance which was found in association with the lesser degrees of epithelial hyperplasia allowed almost constant prediction of the subsequent appearance of this change in the histological sections. The more striking radiological finding of pancreatectasis was encountered in the presence of very extensive epithelial involvement, but had a similar distribution in the secondary ductal system. The reason for the dilatation of the ducts is not entirely clear; nor is it possible to state with confidence the part played by the hyperplastic epithelial changes which are its almost invariable accompaniment. Comparable dilatation of glandular crypts is frequently seen in the wall of the gall-bladder and has been explained on a basis of loss of support or weakening of the wall, combined with abnormal increases in internal pressure (Robertson and Ferguson, 1945). The considerable glandular development found in and around the walls of the dilated pancreatic ducts might allow their expansion in a similar way, although further evidence is required before abnormal secretory pressures can be invoked. In any case, whatever the explanation of the pancreatectasis, the present material did not provide evidence of any local obstructive factor, since the injection medium rarely failed to penetrate into the cysts and moreover, even in examples in which ducts were seen to be completely blocked by intraductal epithelial overgrowth, marked dilatation did not occur (*see Fig.* 147).

The occurrence of intraductal and glandular epithelial hyperplasia in the ampullary region of the main pancreatic duct has been described by Baggenstoss (1938), who referred to the occasional occurrence of "adenomatoid hyperplasia" at this site and found mucosal hyperplasia in 14 of 45 ampullæ examined. The main ampulla was not investigated in the present study, but epithelial changes similar to those described were seen in the ampulla of the accessory duct, where they were frequently responsible for an appearance of irregular filling of the region in the pancreatograms. It appears that the accessory ampulla forms a kind of stagnant backwater in some organs in which the principal outflow occurs through the orifice of the main duct, since the former area was often filled with inspissated secretory material in addition to these epithelial abnormalities. The fact that the accessory duct, although visible in 102 of the pancreatograms, did not appear to be patent in 19 specimens, suggests that the presence of this duct may not reflect its competence to act as an alternative channel for the pancreatic secretion. This is supported by the observation that biliary-pancreatic reflux during cholangiography usually results in a raised serum amylase, an indication of a rise in intraductal pressure which the accessory 'safety-valve' is incapable of preventing (Howell and Bergh, 1950). The present study indicates that even when an accessory pancreatic duct is present and connects with the main ductal system, its ability to allow egress to the duodenum is variable and often inadequate.

The histological picture in the pancreas in the more severe examples of columnar epithelial hyperplasia encountered in the series has a close similarity to that seen in the gall-bladder, for which King and McCallum (1931) introduced the somewhat misleading term "cholecystitis glandularis proliferans". The intramural glands of the ducts of the pancreas (Letulle and Nattan-Larrier, 1898) resemble fairly closely those occurring in the wall of the gall-bladder (Luschka, 1858) and in the common bile-duct (Burden, 1925), in both of which situations glandular proliferation is not uncommon, particularly in the presence of gall-stones or other biliary disease. Such hyperplasia is not invariably accompanied by inflammatory change (Le Quesne and Ranger, 1956), and this was the case in the otherwise normal pancreatic material, for which reason it would appear incorrect to refer to the condition as a pancreatitis. The description 'columnar epithelial hyperplasia' has therefore been used throughout the present article in preference to 'pancreatitis glandularis proliferans'. It is now established that mucosal crypts or diverticula, lined with glandular epithelium and frequently penetrating the full thickness of the wall, occur in approximately 50 per cent of adult gall-bladders (Robertson and Ferguson, 1945). Common variants are extensive localized glandular proliferation, often with the formation of multiple intramural cysts, and superimposed inflammatory changes. Various pathological complications may occur, and these include the formation of small calculi within the intramural crypts (Morgagni, 1769). It is therefore curious that more attention has not been paid in the past to proliferative lesions in the ductal glands of the pancreas and their possible influence upon pathological conditions in that organ. A personal study (Birnstingl, 1958) of the effects of experimental obstruction of the pancreatic ducts in animals has revealed that the intramural glands undergo considerable hyperplasia in that condition, and that the ductal system becomes filled and dilated by their mucinous secretion; a similar process may be observed in malignant obstruction in the human pancreas (Birnstingl, 1959). No evidence has been produced in the present material to explain the wide variation encountered in the development of these structures in normal subjects without demonstrable ductal obstruction, so that, as in the gall-bladder, the cause of the apparent epithelial hyperplasia in these cases remains entirely obscure.

The finding of metaplastic squamous epithelium in the ducts of the pancreas in 8 per cent of the subjects

examined compares closely with the proportion of 8·8 per cent "basal cell metaplasia" reported by Baló and Ballon (1929) in a series of 160 organs from subjects dying without overt pancreatic disease. Like columnar epithelial hyperplasia, with which it is generally associated, it appears that metaplasia occurs so frequently in otherwise normal organs that it should not be considered to be a truly pathological state. Nevertheless, the concomitant finding of areas of pancreatic necrosis in relation to epithelial hyperplasia in five present examples, and the frequent coexistence of obvious structural changes demonstrable by pancreatography, make it necessary to speculate upon the surgical significance of these epithelial lesions. None of the examples in the present series presented clinical evidence of pancreatic disease during life, and this finding accords with that of Rich and Duff (1936), who reported seven specimens showing subclinical necrotic lesions in 150 routine necropsies. Although these workers found the lesions to be apparently associated with squamous metaplasia of small ducts in two of their cases, this has not occurred in the present series. However, columnar epithelial hyperplasia was evident in all of the present five organs in which areas of necrosis were found. Moreover, in two of these specimens small areas of necrosis were seen in close relationship to dilated hyperplastic glandular formations, which strongly suggests that leakage of pancreatic secretion from the ducts may have been responsible for the scattered necrosis. These two series therefore provide evidence that scattered areas of necrosis may be found in association with either metaplastic or hyperplastic epithelial lesions in the pancreas, and have a predominantly interlobular distribution similar to that which has been produced experimentally in animals by obstruction of the ducts at the height of active secretion (Hess, 1909). Acute pancreatic necrosis appears to arise from a variety of causes, which it is not always possible to determine in morbid anatomical material in retrospect. However, in most cases the mechanism depends upon activation of the ferments in the interstitial tissue of the pancreas as a result of wide extravasation during a phase of vigorous secretory activity of the gland, which may occur in the absence of demonstrable obstruction to the outflow. The thin-walled spaces accompanying pancreatectasis and other cystic changes in the ducts and glands would appear to provide an easy exit for such extravasations.

There are few reports of the incidence of epithelial lesions in subjects dying with acute pancreatic necrosis. Rich and Duff examined 24 organs from patients dying with acute hæmorrhagic pancreatitis and found squamous metaplasia in 54 per cent, which he compared with a normal necropsy incidence of 19 per cent. Unfortunately, no estimate was made of the frequency of columnar hyperplasia, which the present study shows to be both commoner and more widely distributed than squamous metaplasia. Yotuyanagi (1936 b) examined three pancreases from subjects dying from acute necrosis and noted papillary and adenomatous proliferation of the ductal epithelium in two of these. He did not relate the epithelial lesions to the causation of the fatal necrosis, although it appears impossible to exclude such a relationship; the main duct of the only patient having no epithelial abnormality contained a round-worm, a sufficient cause for the catastrophe. The occurrence of ductal dilatation and cyst formation in the pancreas and its ready demonstration by pancreatography are insufficiently recognized. Great interest will therefore attach to future studies concerning the incidence of these structural changes in cases of acute pancreatic necrosis.

Further evidence is also required to clarify the association between epithelial hyperplasia and chronic pancreatic disease. Yotuyanagi (1936 b) studied the histology of the pancreas in 18 subjects with various types of chronic disease affecting the organ. He found severe "ductogenous pancreatic fibrosis", a picture similar to that seen in chronic relapsing pancreatitis, in 5 of these which, with one exception, was accompanied by very widespread and advanced glandular and intraductal epithelial proliferation. Edmondson, Bullock, and Mehl (1949, 1950) encountered "an unusual epithelial hyperplasia" of the ducts in some of their cases of pancreatic lithiasis and calcification, which appear from the illustrations accompanying their articles to have been typical columnar epithelial hyperplasia associated with ductal dilatation. These authors did not record the incidence of the hyperplasia, nor, apparently, did they associate it with the occurrence of the calcification, but their report of the finding of micro-calculi within small epithelial-lined spaces and in masses of inspissated secretion within the ducts, suggests that the two conditions may have been related. Dilated cystic spaces and accumulations of inspissated material are common accompaniments of epithelial hyperplasia and could provide a convenient nidus for the origin of intraductal calcification. This explanation accords with the observation that it is exceptional for pancreatic calcification to occur within the parenchyma and that it usually takes place within the ducts (Edmondson and others, 1950).

In view of the wide range of radiographic and histological appearances encountered in the present study of apparently normal necropsy material, it is evident that pancreatograms obtained during abdominal surgery need to be interpreted with caution. Nevertheless, the procedure appears to reflect closely the configuration of the ductal system and its morbid anatomical variants. Some of the appearances obtained in the present investigation in association with ductal and glandular epithelial hyperplasia closely resemble those reported in patients suffering from chronic relapsing pancreatitis (Leger and Bréhant, 1956; Doubilet and others, 1957), and further radiographic studies in the living subject and at necropsy will undoubtedly elucidate the part played by epithelial changes in the pathology of pancreatic disease.

SUMMARY

1. As a result of combined radiographic and histological study in necropsy material, the common anatomical variations which influence the interpretation of pancreatograms have been reviewed. The main pancreatic duct showed variation in calibre ranging between maximum diameters of 1·8 and 9·2 mm.; it appears that the upper limit of the normal diameter of this duct is about that of an ordinary lead pencil (8 mm.). Appearances of isthmic stenosis, terminal dilatation, and an undulating outline in this

duct were occasionally seen and represent anatomical variants. The accessory pancreatic duct communicated with the main ductal system in 68 per cent of specimens, but only appeared patent in 55 per cent.

2. Dilatation and irregularity of the secondary pancreatic ducts was commonly seen on the pancreatograms and produced an appearance of pancreatectasis in a few specimens. These variations closely reflected the development of hyperplastic and metaplastic changes in the ductal epithelium.

3. Columnar epithelial hyperplasia was seen in 29 per cent of organs; the change was most frequent in the secondary ducts and in the ampullary region of the accessory pancreatic duct. It was most common in the form of intraductal proliferation, but hyperplasia of mucus-secreting glandular structures related to the ducts was also seen. These variants resemble cholecystitis glandularis proliferans, with which they are comparable. Subclinical focal pancreatic necrosis was encountered in five specimens, in which it was apparently related to the presence of hyperplastic epithelial lesions in the ducts.

4. Squamous epithelial metaplasia was present in 10 per cent of organs, although never to the extent shown by columnar hyperplasia, with which the change was generally associated.

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REFERENCES

BAGGENSTOSS, A. (1938), *Arch. Path., Chicago*, **26**, 853.
BALO, J., and BALLON, H. C. (1929), *Ibid.*, **7**, 27.
BIRNSTINGL, M. A. (1958), *M.S. Thesis, University of London.*
— — (1959), *Brit. med. J.*, **1**, 938.
BURDEN, V. G. (1925), *Ann. Surg.*, **82**, 584.
CORDIER, G., and ARSAC, G. (1952), *J. Chir., Paris*, **68**, 505.
DOUBILET, H., POPPEL, M. H., and MULHOLLAND, J. H. (1957), *J. Amer. med. Ass.*, **163**, 1027.
EDMONDSON, H. A., BULLOCK, W. K., and MEHL, J. W. (1949), *Amer. J. Path.*, **25**, 1227.
— — — — — — (1950), *Ibid.*, **26**, 37.
HESS, O. (1909), *Mitt. Grenzgeb. Med. Chir.*, **19**, 637.
HOWELL, C. W., and BERGH, G. S. (1950), *Gastroenterology*, **16**, 309.
KING, E. S. J., and MCCALLUM, P. (1931), *Brit. J. Surg.*, **19**, 310.
KORPÁSSY, B. (1938), *Virchows Arch.*, **303**, 359.
LEGER, L., and BRÉHANT, J. (1956), *Chirurgie du Pancréas.* Paris: Masson.
LETULLE, M., and NATTAN-LARRIER. (1898), *Bull. Soc. anat. Paris*, **73**, 491.
Le QUESNE, L. P., and RANGER, I. (1956), *Brit. J. Surg.*, **44**, 447.
LERICHE, R. (1930), *Bull. Soc. nat. Chir.*, **56**, 1316.
LUSCHKA, H. (1858), *Z. rat. Med.*, **4**, 189.
MORGAGNI, J. B. (1769), *The Seats and Causes of Diseases investigated by Anatomy*, **2**, 235. London: Millar & Cadell.
NEWMAN, H. F., WEINBERG, S. B., NEWMAN, E. B., and NORTHUP, J. D. (1958), *Surg. Gynec. Obstet.*, **106**, 687.
REINHOFF, W. F., and PICKRELL, K. L. (1945), *Arch. Surg., Chicago*, **51**, 205.
RICH, A. R., and DUFF, G. L. (1936), *Bull. Johns Hopk. Hosp.*, **58**, 212.
ROBERTSON, H. E., and FERGUSON, W. J. (1945), *Arch. Path. (Lab. Med.)*, **40**, 312.
STEIN, A. A., and POWERS, S. R. (1956), *Ibid.*, **62**, 494.
WAINWRIGHT, C. W. (1951), *New Engl. J. Med.*, **244**, 161.
YOTUYANAGI, S. (1936 a), *Mitt. allg. Path., Sendai*, **9**, 403.
— — (1936 b), *Ibid.*, **9**, 337.

PAPILLARY CYSTADENOCARCINOMA OF THE PANCREAS
WITH REPORT OF TWO CASES

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MACROSCOPIC cysts of the pancreas are uncommon and neoplastic cysts are rare. Hale-White (1897) found only 3 cases of pancreatic cyst among 6708 autopsies at Guy's Hospital, London. None was a cystadenoma or cystadenocarcinoma. Miller, Baggenstoss, and Comfort (1951) found only one cystadenocarcinoma among 202 carcinomas of the pancreas, excluding islet-cell tumours, autopsied at the Mayo Clinic between 1920 and 1946. In 8500 autopsies at the Postgraduate Medical School, London, between 1935 and 1958, there were 76 cases of primary solid carcinoma of the pancreas and 5 pancreatic cysts (*Table I*). Two of these cysts, reported below, were papillary cystadenocarcinomas. After a search through the literature we have been able to find only 16 adequately documented cases. These 18 cases form the basis of our report.

Table I.—CYSTIC LESIONS OF PANCREAS IN 8500 AUTOPSIES

TYPE	SITE	SEX	AGE
Papillary cystadenocarcinoma	Tail	F.	69 yr.
Papillary cystadenocarcinoma	Body	F.	49 yr.
Metastatic cystic adenocarcinoma	Tail	F.	59 yr.
Teratomatous cyst	Head	F.	15 hr.
Hydatid cyst	Tail	F.	32 yr.

CASE REPORTS

Case 1.—Mrs. L. G., aged 36 years, was first seen at Hammersmith Hospital in October, 1944, complaining of intermittent attacks of epigastric pain for the past three to four years. The pains came on one to two hours after a meal and were associated with some nausea. The patient had a good appetite. Physical examination revealed no abnormality. A chest radiograph was normal. Plain radiographs of the abdomen showed a small opacity in the right renal area which was thought to be a renal calculus. Barium meal showed some deformity of the duodenal cap, but no ulcer could be demonstrated. She was given medical treatment for a duodenal ulcer with only slight improvement. In 1945 she was still complaining of occasional attacks of epigastric pain. In 1948 she had a repair of a prolapsed uterus. In 1951 she again attended the out-patients' clinic complaining of epigastric pains and indigestion. She was put on a peptic ulcer régime with considerable improvement. In February, 1956, she was treated for a fronto-ethmoidal abscess. Examination of the abdomen showed no abnormality.

In October, 1956, she complained of pain in the left side of the chest and in the back. In November, 1956, she was admitted to hospital complaining of continuous epigastric pain unrelieved by food or alkalis.

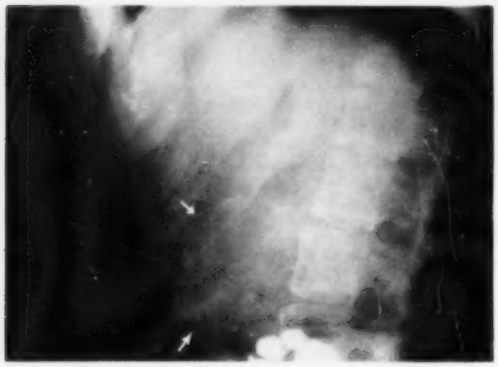

FIG. 155.—Calcified rim of pancreatic cyst.

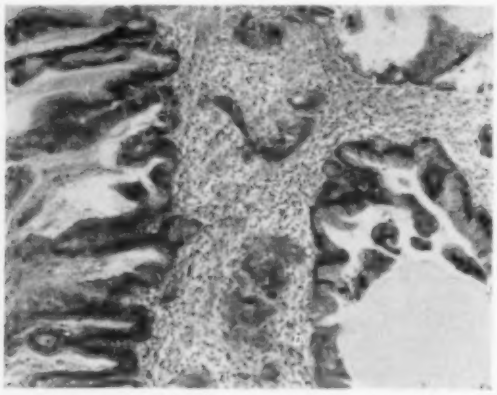

FIG. 157.—*Case* 1. Papillary mucus-secreting adenocarcinoma with solid undifferentiated tumour in centre. H. and E. (× 66.)

ON EXAMINATION.—A firm mass which moved slightly with respiration was palpable in the left upper quadrant of the abdomen just beneath the costal margin. A plain radiograph of the abdomen showed a spherical shadow with marginal calcification lying anterior to the left kidney and just below the spleen (*Fig.* 155). Barium meal showed a constant filling defect on the greater curve of the stomach (*Fig.* 156). The mucosal pattern was intact. The defect was attributed to extraneous pressure, possibly due to a splenic artery aneurysm or pancreatic neoplasm. Stomach emptying began at once. The duodenum was normal. There was also evidence of the presence of a small gall-stone. Chest radiograph was normal. Hæmoglobin 86 per cent (Haldane). W.B.C. 8000 per c.mm. with normal differential; plasma bilirubin 0·5 mg. per cent; serum alkaline phosphatase 4·2 K.-A. units per cent; thymol turbidity 1·5 units; plasma proteins 7·5 g. per cent, albumin 3·9 g. per cent, globulin 3·6 g. per cent; W.R. and Kahn negative; blood-urea 25 mg. per cent; urine normal.

FIG. 156.—Barium meal. Extrinsic filling defect on greater curve.

AT OPERATION.—A laparotomy was performed on Nov. 23, 1956 (Professor Ian Aird). A large cystic mass was found in the middle of the pancreas. The splenic artery was attenuated over its upper border. The splenic vein was obliterated. The spleen and splenic artery were mobilized from the posterior abdominal wall and were removed with that part of the pancreas lying left of the origin of the superior mesenteric artery. There was a palpable extension of the swelling in the region of the common bile-duct which it was not feasible to remove. No metastases were seen or felt in the liver.

PATHOLOGICAL EXAMINATION.—The specimen consisted of the spleen, with the tail and body of the pancreas. The spleen appeared normal. At the junction of the tail and body of the pancreas there was a rounded cystic tumour, 8 × 7 × 6 cm., with a fairly smooth surface. On

section there was a fibrous, partly calcified wall, up to 7 mm. in thickness. The cyst was multiloculated, containing pale, somewhat papillary tissue and thick mucoid fluid. Microscopic study shows the wall of the cyst to consist of a thick layer of fibrous connective tissue containing traces of calcium even after decalcification. No smooth muscle is present in the capsule or stroma. Within this wall there is a papillary tumour lined with tall columnar

FIG. 158.—*Case* 2. Unilocular cyst in pancreatic tail. Flattened papillæ in the cyst lining are visible in the lower half of the photograph.

mucin-secreting cells with basal nuclei (*Fig.* 157). There are also several lumina lined with the same type of epithelium. In some areas, however, an anaplastic tumour is growing from this epithelium and consists of strands and masses of rather large irregular cells. These cells have abundant eosinophilic cytoplasm and large nuclei with prominent nucleoli. Numerous mitoses are present. There are also some tumour giant cells with hyperchromatic nuclei. In some areas there is extensive necrosis. Tumour can be seen invading the wall of the cyst and spreading into the tissues outside. The tumour growing out from the cyst is composed of pleomorphic carcinoma.

PROGRESS.—Following the operation the patient suffered from continuous dull aching pain in the back and on both sides of the abdomen. The wound discharged pus through a drainage tube. She ran an irregular pyrexia and had a high leucocyte count. Jaundice became marked one month after operation and a mass appeared in the right hypochondrium. This was regarded as a distended gall-bladder due to obstruction of the common bile-duct. A laparotomy was performed on Jan. 12, 1957. The surface of the liver was studded with secondary tumour deposits. The palpable mass was found to be tumour on the under-surface of the liver. The gall-bladder appeared normal. There was no extrahepatic biliary obstruction. The abdomen was closed. The patient died thirty-six hours later. At autopsy, tumour masses were present in the operation bed and metastases were found in the liver, lungs, and both pleuræ. The head of the pancreas was normal.

Case 2.—Mrs. E. B., aged 69 years, was first seen at Hammersmith Hospital in July, 1958. She complained of pain in the back for six months, pain in the left calf for eight weeks, and generalized abdominal pains, maximal in the epigastrium, for the previous three weeks. She also complained of nausea, some vomiting, loss of appetite, and recent weight-loss. There was nothing significant in her past medical or family history.

ON EXAMINATION.—She had a sallow complexion and showed evidence of recent weight-loss. An enlarged liver with a firm irregular edge could be felt. A firm mass which moved slightly with respiration was palpable just below the left costal margin. The left calf was swollen and tender and the superficial veins were dilated. Investigations showed hæmoglobin 69 per cent (Haldane); W.B.C. 9000 per c.mm. with normal differential; plasma bilirubin 1·8 mg. per cent; direct van den Bergh test positive; serum alkaline phosphatase 22 K.-A. units per cent; thymol turbidity 1 unit; plasma proteins 6·5 g. per cent, albumin 2·4 g. per cent, globulin 4·1 g. per cent;

FIG. 159.—*Case* 2. Section through one of the papilliferous excrescences shown in *Fig.* 158. (× 6·4.)

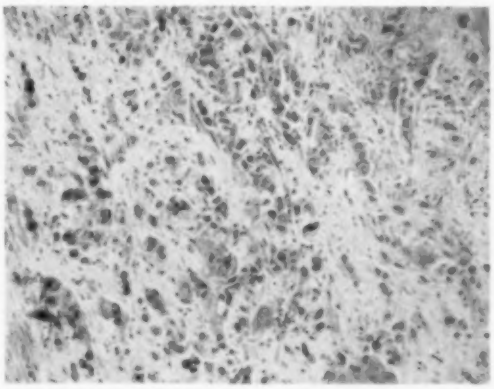

FIG. 160.—*Case* 2. Pleomorphic appearance of tumour in tissue behind pancreas. (× 102.)

W.R. and Kahn negative; urine normal. Radiographs of dorsal and lumbar spine showed slight hypertrophic lipping only. The provisional diagnosis was carcinoma of the stomach with hepatic metastases. The patient was considered too ill for laparotomy and died four weeks after admission to hospital.

POST-MORTEM EXAMINATION.—At autopsy there was swelling of the left leg. The inferior vena cava and the deep veins of the left leg contained firm laminated thrombus slightly adherent to the vessel walls. There was a large rounded, tense, thick-walled cyst, approximately 13 cm. in diameter, in the tail of the pancreas (*Fig.* 158). On section it had a firm white capsule varying in thickness between 3 and 8 mm. The cyst was unilocular with small, fleshy, rather mushroom-shaped nodules of tumour projecting inwards from its wall. It was filled with a thick grey mucinous fluid. The head and body of the pancreas and Wirsung's duct appeared normal. Tumour deposits could be seen in the neighbouring lymph-nodes, peritoneum, and omentum. Metastases were also found in the liver, kidneys, diaphragm, lungs,

left pleural cavity, pericardium, thyroid, adrenals, and vertebral bone-marrow.

Microscopic study shows a papillary cystadenocarcinoma of the pancreas with infiltration of tumour through the cyst wall into the surrounding tissues. The cyst wall consists of a thick fibrous capsule containing small foci of calcification. No smooth muscle-fibres are seen. Dilated thin-walled blood-vessels are numerous in the outer layer of the capsule. A few compressed pancreatic acini, distorted ducts, and islets of Langerhans can be seen in the outer layers. The cyst wall is incompletely lined with a tall columnar mucin-secreting epithelium with basal nuclei. In several places this epithelium has proliferated and papillary tumour masses project into the cyst cavity (*Fig.* 159). The papillæ are long and slender with fine connective tissue cores. The covering epithelium consists mainly of a single layer of tall columnar cells, but at the bases of the tumour masses, close to the cyst wall, the tumour is less well differentiated and the papillæ are lined with two or more layers of cells. Occasional mitoses with some atypical forms are seen. The tumour has invaded the cyst wall and spread into the surrounding tissues. In the fibrous wall the carcinoma cells are grouped in small follicles and solid trabeculæ. The cells appear more pleomorphic away from the cyst cavity and in the tissues around the pancreas many tumour cells have a bizarre appearance (*Fig.* 160). These cells are large and pleomorphic and have abundant eosinophilic cytoplasm and distorted nuclei. The cytoplasm is sometimes vacuolated, and slender processes extend from some of the more spindle-shaped cells. The nuclei are often hyperchromatic and contain one or two large eosinophilic nucleoli. A few multinucleated giant cells are present. The head and body of the pancreas appear normal apart from some post-mortem autolysis. Sections from the metastases

Table II.—Data in Reported Cases of Cystadenocarcinoma of Pancreas

Author	Year	Sex	Age	Site	Operation	Follow-up	Pathology
Kaufmann	1929	F.	47	Tail	None	Died	Autopsy: Cyst size of fist. Metastases liver and omentum
Lichtenstein	1934	F.	44	Tail	None	Died 6 yr. after onset of illness	Autopsy: Multilocular cyst. Metastases liver, omentum, and peritoneum
Baehr and Klemperer	1936	F.	52	Body	None	Died 2 yr. 10 mth. after onset of illness	Autopsy: Multilocular cyst size of grapefruit. Metastases lymph-nodes and liver
Young	1937	F.	34	—	Partial excision and marsupialization	Died 7 yr. later. Sinus track persisted	Large multilocular cyst. Biopsy sinus track before death showed adenocarcinoma. No autopsy
Kennard	1941	F.	40	Body	Enucleated	Well 10 mth. later	Multilocular cyst 15 cm. diameter
Hartz and van der Sar	1946	F.	56	Tail	None	Died 8 mth. after onset of illness	Autopsy: Cyst 6 cm. diameter. Metastases in liver
Burk and Hill	1952	F.	39	Body	Enucleated	Well 3 yr. later	Multilocular cyst 18 cm. diameter
Sawyer, Spencer, and Lubchenco	1952	F.	58	Tail or body	Distal pancreatectomy	Died 2 mth. after admission	Cyst 10 cm. diameter. At subsequent laparotomy metastatic adenocarcinoma in liver. No autopsy
Willis	1953	F.	45	Tail	Laparotomy	Died	Autopsy: Rounded cyst 10 cm. diameter. Metastases lymph-nodes, liver, lungs, and kidneys
Cattell and Warren	1953	F.	51	Body	Distal pancreatectomy	Alive, but failing rapidly 2 yr. later	Cyst 12 cm. diameter
		F.	38	Body and tail	Distal pancreatectomy	Well 2 yr. later	Multilocular cyst 12 cm. diameter
		F.	48	Body and tail	Distal pancreatectomy	Well 6 mth. later	Multilocular cyst 12·5 × 5·5 × 4 cm.
		M.	49	Head and body	Laparotomy and biopsy. Later total pancreatectomy	Well 4 mth. later	Biopsy adenocystoma. Specimen large cystadenocarcinoma
Mason, DeGiorgio, and McGrath	1954	F.	64	Head	Enucleated	Well nearly 1 yr. later	Multilocular cyst 12·5 × 10 × 10 cm.
Gwynne and Wilson	1956	F.	45	—	Enucleated	Well 2 yr. 9 mth. later	Multilocular cyst 7 cm. diameter
Rutledge and Lischer	1958	F.	26	Body and tail	Distal pancreatectomy	Died 2 mth. later	Multilocular cyst 18 × 13 × 8 cm. No autopsy
Cornes and Azzopardi *Case* 1	1959	F.	48	Body	Distal pancreatectomy	Died nearly 2 mth. later	Multilocular cyst 8 × 7 × 6 cm. Autopsy: Metastases lymph-nodes, liver, and lungs
Case 2		F.	69	Tail	None	Died 1 yr. after onset of illness	Autopsy: Unilocular cyst 13 cm. diameter. Metastases lymph-nodes, liver, kidneys, diaphragm, lungs, thyroid, adrenals, and spine

show areas of papillary and follicular mucin-secreting adenocarcinoma and areas of pleomorphic carcinoma.

DISCUSSION

Lichtenstein (1934) reported what he believed to be the first authentic case of cystadenocarcinoma of the pancreas recorded in America. After a careful study of the literature he was able to find only one other reasonably well documented case, that of Kaufmann (1929). Kennard (1941) described one case of papillary cystadenocarcinoma and listed 24 other possible cases. He included 13 cases which had been previously considered by Lichtenstein and discarded on the basis of incomplete study and documentation. A similar criticism can be made of several other cases listed by him. Since 1941 we have found reports of 11 well documented cases. Including the two cases here reported the number of reasonably documented cases amounts to only 18 (*Table II*). We have included in *Table II* all cases in which the pathological diagnosis stands up to critical scrutiny and in which sufficient clinical data are available, in order to obtain a true reflection of the biological features of this neoplasm. Lack of such discrimination has led to erroneous evaluation of the sex incidence, localization, and other properties of this tumour. Cases with inadequate histological confirmation or in which there is doubt about the primary seat of the neoplasm are omitted. Similarly, cases where a carcinoma may have merely coexisted with pancreatic cyst or where cystic change could have been the result of secondary degeneration in a tumour have been eliminated. Finally, some cases of probable cystadenocarcinoma have been excluded because of inadequate data, clinical or pathological. Sommers and Meissner (1954) in a study of the microscopical appearances of unusual carcinomas of the pancreas mention 3 cases of papillary cystadenocarcinoma, but omit data on the individual cases. Smith (1953) describes a case of cystadenocarcinoma of the pancreas with unusual clinical features and histological appearance.

It will be seen from *Table II* that, unlike primary solid pancreatic carcinomas, these tumours occur mainly in women. They are found in a younger age-group than primary solid carcinomas, two-thirds of the patients listed being under 50 years of age, and they are situated chiefly in the tail and body of the pancreas. *Table III* shows a comparison between the cystadenocarcinomas mentioned in *Table II* and 76 cases of primary solid carcinoma autopsied in this school. Ampullary carcinomas and carcinomas of the extrahepatic bile-duct involving the head of the pancreas have as far as possible been excluded from the table. The mean ages are not strictly comparable as the figure for solid carcinomas refers to age at autopsy while the figure for the cystic lesions is drawn chiefly from surgical material. Allowing for this there is still a difference of about ten years in the mean age. Cystadenocarcinoma thus appears to have the same sites of origin, age, and sex incidence as Benson and Gordon (1947) described for cystadenoma.

Table III.—Comparison of Primary Solid Pancreatic Carcinoma and Cystadenocarcinoma

Type	No. of Cases	Men	Women	Mean Age	Head	Body and Tail	Not known
Solid carcinoma	76	46	30	62·1 (½ over 58 yr.)	45	28	3
Cystadeno-carcinoma	18	1	17	47·4 (½ under 50 yr.)	2	14	2

Clinical Features.—The main symptoms are epigastric pain and indigestion. Some of the patients had nausea and several complained of lumbar pains. A few patients presented simply with abdominal swelling or a palpable mass in the abdomen slowly increasing in size. When the tumour has spread beyond the capsule the presenting symptoms may be caused by distant metastases, as in our *Case* 2. Physical examination may fail to show any abnormality. A mass may be felt in the upper abdomen, usually on the left side, and often extending up under the left costal margin. As the tumour is most often in the tail and body, it generally moves slightly with respiration. Plain radiographs of the abdomen may show soft-tissue shadows, and areas of calcification may be seen, as in our first case and that of Rutledge and Lischer (1958). Barium-meal and barium-enema studies may show a mass between the stomach and the transverse colon, pushing the transverse colon downwards and forwards; the greater curve of the stomach may be indented and the stomach itself pushed anteriorly and to the right, and either upwards or downwards (Haukohl and Melamed, 1950). There is usually no evidence of any endocrine disturbance, though in the case described by Kennard (1941) there was a trace of glycosuria.

Pathology.—The cystadenoma is an encapsulated tumour which may be multilocular or unilocular, papillary or non-papillary (Glenner and Mallory, 1956). Its cavities contain a serous or mucoid fluid which may contain pancreatic ferments. The loculi are usually lined with a single layer of cuboidal or flattened cells; sometimes they are lined with columnar cells with small, dark, basal nuclei and a pale-staining cytoplasm.

The cystadenocarcinoma is likewise encapsulated, but the capsule may be obscured in part by neoplastic invasion. It consists of hyaline fibrous tissue, but its outer layers contain many thin-walled vessels which may cause troublesome bleeding at operation. The capsule of the tumour is surrounded by a false capsule of compressed pancreatic tissue, giving a plane of cleavage which permits enucleation of the cyst. Like its benign counterpart, the fibrous stroma including the capsule often shows calcification. The cystic contents are mucoid and may contain altered blood. The presence of diastase in the fluid has been noted by Lichtenstein (1934), Burk and Hill (1952), and Willis (1953). Papillary ingrowths of the lining epithelium are frequently seen, and while indicative of proliferative activity, are not by themselves sufficient for a diagnosis of malignancy in a cystadenoma of dubious appearance. In the absence of metastases, perineural invasion, extracapsular extension, areas of frank anaplasia, or other unequivocal evidence of malignancy, evidence of malignant

change must be sought in the presence of focal areas showing pseudostratification or true stratification, nuclear hyperchromasia and irregularity, increase in nuclear size, mitotic activity, etc. Such criteria are not unlike those utilized in the interpretation of a pseudomucinous ovarian cyst of borderline malignancy. Histological evidence of malignancy of this sort is seen in the cases of Mason, DeGiorgio, and McGrath (1954) and Kennard (1941). In more obviously malignant cases, solid carcinomatous clumps infiltrate the connective tissue stroma (*see Fig.* 157), and anaplastic areas with bizarre tumour cells and neoplastic giant cells may be seen (*see Fig.* 160). Tumours with such pleomorphic appearances are reported by Hartz and Van der Sar (1946), Willis (1953), and Sommers and Meissner (1954). Sommers and Meissner draw attention to the resemblance of such anaplastic areas to malignant melanoma, pleomorphic rhabdomyosarcoma, and other tumours in which an abundant eosinophilic cytoplasm is often a conspicuous feature. Examination of tumour from such areas alone may lead to lack of recognition of the nature of the primary neoplasm.

The overall appearance of cystadenoma and cystadenocarcinoma, the similarity in localization, age, and sex incidence suggest the possibility of the malignant lesion developing from a pre-existing cystadenoma. The presence in the malignant tumours of areas microscopically indistinguishable from those seen in the benign tumour lends some support to this view. Cases are on record in which there was evidence of the presence of a lesion many years before the appearance of a definitely malignant tumour (Lichtenstein). In some cases histological confirmation of the benignity of the original neoplasm was available (Young, 1937). It is probable that most cystadenocarcinomata of the pancreas arise on the basis of a pre-existing benign tumour.

The histogenesis of pancreatic cystadenocarcinoma involves consideration of the origin of the cystadenoma. All the evidence suggests that the latter is a neoplasm of pancreatic ducts (Glenner and Mallory, 1956). The view that this lesion arises from misplaced included tissues of diverse origin or from embryonic structures is superfluous. The abundant mucin produced by these tumours is merely an exaggeration of a function possessed by normal pancreatic ducts; such an exaggeration is a well-known feature of many benign and malignant tumours in other regions of the body.

Treatment.—Since most of these tumours occur in the tail and body of the pancreas, they can be removed and the head spared. When this is possible there is a strong chance of a good result. When situated in the head, standard pancreaticoduodenectomy, as done for capital and ampullary tumours, may be attempted with re-implantation of the transected body into the jejunum. On some occasions (Burk and Hill, 1952; Gwynne and Wilson, 1956), a cystic tumour thought to be benign has been enucleated, with survival for a few years at the time of reporting, in spite of a histological diagnosis after the operation of intracystic malignant disease. According to Smith (1953) there is no evidence that radiotherapy has anything to offer in the treatment of these neoplasms.

SUMMARY

1. Pancreatic cysts are uncommon. Five pancreatic cysts were found in 8500 autopsies. Neoplastic cysts are rare.

2. Two cases of papillary cystadenocarcinoma of the pancreas are described and data relating to 16 other cases collected from the literature are tabulated.

3. In contrast to primary solid carcinomas, they occur in a younger age-group, mainly in women, and are found most commonly in the tail and body of the pancreas.

4. Cystadenocarcinoma is a mucus-secreting tumour arising from pancreatic duct epithelium. It is probable that many cases arise from a pre-existing benign cystadenoma. Tumour that has spread beyond the cyst wall may have an undifferentiated or pleomorphic microscopical appearance; biopsy of such an area may lead to the nature of the primary lesion being missed.

5. It is sometimes impossible to say at laparotomy whether a given cystic tumour is benign or malignant. Excision rather than enucleation is therefore advisable.

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REFERENCES

BAEHR, G., and KLEMPERER, P. (1936), *J. Mt Sinai Hosp.*, **3**, 48.
BENSON, R. E., and GORDON, W. (1947), *Surgery*, **21**, 353.
BURK, L. B., and HILL, R. P. (1952), *Ann. Surg.*, **136**, 883.
CATTELL, R. B., and WARREN, K. W. (1953), *Surgery of the Pancreas*, 179, 191, 340. Philadelphia: W. B. Saunders.
GLENNER, G. G., and MALLORY, G. K. (1956), *Cancer*, **9**, 980.
GWYNNE, J. F., and WILSON, S. L. (1956), *Aust. N.Z. J. Surg.*, **26**, 315.
HALE-WHITE, W. (1897), *Guy's Hosp. Rep.*, **54**, 17.
HARTZ, P. H., and VAN DER SAR, A. (1946), *Amer. J. clin. Path.*, **16**, 219.
HAUKOHL, R. S., and MELAMED, A. (1950), *Amer. J. Roentgenol.*, **63**, 234.
KAUFMANN, E. (1929), *Pathology for Students and Practitioners* (trans. Reimann), vol. 2, 1045. London: H. K. Lewis.
KENNARD, H. E. (1941), *Surgery*, **9**, 65.
LICHTENSTEIN, L. (1934), *Amer. J. Cancer*, **21**, 542.
MASON, L. W., DEGIORGIO, E. R., and MCGRATH, F. L. (1954), *J. int. Coll. Surg.*, **22**, 440.
MILLER, J. R., BAGGENSTOSS, A. H., and COMFORT, M. W. (1951), *Cancer*, **4**, 233.
RUTLEDGE, R., and LISCHER, C. E. (1958), *Texas St. J. Med.*, **54**, 89.
SAWYER, K. C., SPENCER, J. R., and LUBCHENCO, A. E. (1952), *Ann. Surg.*, **135**, 549.
SMITH, R. (1953), *The Surgery of Pancreatic Neoplasms*, 89, 128. Edinburgh: Livingstone.
SOMMERS, S. C., and MEISSNER, W. A. (1954), *Arch. Path. (Lab. Med.)*, **58**, 101.
WILLIS, R. A. (1953), *Pathology of Tumours*, 2nd ed., 447. London: Butterworth.
YOUNG, E. L. (1937), *New Engl. J. Med.*, **216**, 334.

PANCREATITIS FOLLOWING GASTRECTOMY

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Pancreatitis is always serious when it follows gastrectomy, particularly when it occurs in the early post-operative period. Death would appear to occur sooner in the hæmorrhagic type, but this may merely be an indication of the greater severity of this type. Pancreatitis may be associated with, or be the cause of, wound disruption, suppression of urine, or pulmonary complications, and these tend to confuse the diagnosis. Most of the cases occur in the first ten days after operation but may be delayed for many weeks, months, or years.

INCIDENCE AND MORTALITY

In a series of 1689 gastrectomies reported by Burton, Eckman, and Haxo (1957) there were 94 deaths, 12 of which were due to pancreatitis (12·7 per cent or 0·7 per cent of the total). Collected figures from various authors show that in 128 cases of post-gastrectomy pancreatitis the mortality was 55·5 per cent. The true incidence of this complication is difficult to ascertain because the less severe cases are probably not diagnosed.

CAUSATION

Claude Bernard produced pancreatitis in 1856 by injecting bile and sweet oil into the pancreatic ducts of cats. Opie in 1901 demonstrated at autopsy a small stone in the ampulla of Vater in a case of pancreatitis where there was a common channel between the termination of the common bile-duct and the pancreatic ducts. Popper and Necheles (1951) have shown experimentally in dogs that severe injuries to the pancreas inhibit secretion and pancreatitis does not occur, whereas it may occur after the production of minor lesions.

Millbourn (1949) has shown that in 90 per cent of cases the duct of Wirsung serves as the sole or chief excretory channel of the pancreas, but in 10 per cent of cases the accessory duct of Santorini is the main or only excretory channel. This latter duct is more liable to injury during gastrectomy since it lies nearer the surface and opens into the duodenum nearer the pylorus than the duct of Wirsung. Milbourne describes a case of fatal post-gastrectomy pancreatitis in which the duct of Santorini was found to have been inadvertently tied during mobilization of the duodenum.

Pancreatitis seems to depend on activated pancreatic enzymes coming into contact with pancreatic tissue. This might occur if the pancreatic ducts had ruptured or the secretions had been forced through the wall of the ducts. Another possible cause might be the reflux of activated enzymes from the duodenum into the ducts, in which case the pancreas would have to be capable of active secretion.

Howell and Bergh (1950) investigated radiologically and biochemically patients with T-tube drainage of the common bile-duct. They showed that 5 out of 6 patients with pancreatitis had reflux up the pancreatic duct, and 25 out of 27 patients showing reflux had serum levels above 200 Somogyi units (normal 60–180), while 37 of 38 patients with no reflux had serum amylase levels below 200 after investigation. This would suggest that the reflux of bile alone into the pancreatic duct may play a part, possibly by activating pancreatic enzymes.

Obstruction of the pancreatic ducts due to spasm of the sphincter of Oddi, or sludging of the pancreatic juices post-operatively, or by the long limb of a T-tube passing through the ampulla, have also been blamed, but their action may be to cause reflux of bile into the pancreas.

During two operations for post-gastrectomy acute obstruction of the afferent loop, one of the authors (N. C. T.) has noted severe pancreatic œdema in one and œdema with escape of pancreatic juice in the other. It occurred to him that the cause of those cases might have been the reflux of the obstructed duodenal juices into the pancreas as a result of the increased intraduodenal pressure. This possibility is made more likely by the fact that in Tanner's series no case of pancreatitis had arisen for the first time after the Billroth-I (gastroduodenal) form of anastomosis, in which severe dilatation of the duodenum does not occur. Other observers have noted an increase in the blood-amylase in cases of experimental intestinal obstruction in which the second part of the duodenum becomes dilated.

It might be expected that most cases of pancreatitis would follow a difficult dissection of the duodenum or stomach from the pancreas damaging small or large pancreatic ducts, or allowing the leakage of pancreatic juices from a crater which had eroded into a duct. Such cases are recorded, but in the experience of one author (N. C. T.), all his cases of pancreatitis occurred where there was no pancreatic penetration, or any difficult duodenal dissections.

DIAGNOSIS

Severe post-gastrectomy complications may be insidious or catastrophic in onset and are notoriously difficult to diagnose with certainty.

Pain may be slight, though it can be severe and associated with profound collapse. Abdominal tenderness and increasing rigidity are usually present, but are difficult to distinguish from wound tenderness or muscle cramps and they may be obscured by analgesics. Vomiting may occur, but in most cases is prevented by the presence or early use of an intragastric tube. There is occasionally backache, though this may also be present in acute afferent loop obstruction.

Later complications assume a prominent aspect. A mass may appear usually in the left lumbar region. Suppression of urine has been recorded. Tetany may follow the hypocalcæmia associated with fat necrosis and saponification. Rarely will hyperglycæmia and glycosuria arise. Prolonged suppuration may lead to a slow and steady deterioration of the patient.

In diagnosis, the serum and urinary amylase give help if they are very markedly raised, but they will depend on the stage of the disease. The levels are high at the onset, but with total necrosis of the pancreas they are sometimes little raised. Series of

amylase levels before and after routine gastric surgery have shown varying results. McKenzie (1954) reports 400 cases, only 3 of which showed any rise after operation, and Dunphy, Brooks, and Ackroyd (1953) 50 cases in which there was a transient rise in 3 only. Mahaffey and Howard (1955), on the other hand, showed a rise in 7 of 20 cases, in 3 more than 100 per cent above normal, but in 8 the amylase almost disappeared. The senior writer has also carried out a series of post-gastrectomy serum amylase values and found that slight rises may occur, but rises to great levels (1000) are very rare.

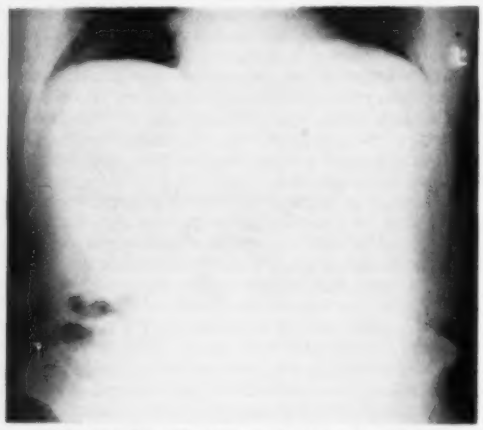

FIG. 161.—Dense shadow in left subphrenic region in a patient with sudden pain and collapse 5 days after gastrectomy. It was due to the presence of blood from a 'delayed splenic rupture'.

The differential diagnosis is difficult. The serum amylase may be raised in suture line leakage, acute afferent loop obstruction (which may coexist with pancreatitis), or small bowel obstruction.

A straight radiograph helps to differentiate obstructive lesions, free perforation, and post-operative splenic rupture (giving a dense shadow in the left hypochondrium) (*Fig.* 161). After recovery, areas of calcification may be seen in or near the pancreas. Chest radiograph excludes bilateral pulmonary collapse, and an electrocardiogram may be required to exclude acute coronary artery infarction. Acute infarction is not a common post-operative complication though it can occur at any time. (A case of one of the authors (N. C. T.) died of acute coronary occlusion five hours *prior* to the time fixed for operation.)

Because some cases of pancreatitis have occurred as a result of direct damage to the pancreas, the pancreas should be handled as gently as possible and incisions into the gland avoided. Dissection close to the duodenum will minimize damage to the head of the pancreas. Large penetrating duodenal ulcers may be treated by the Bancroft or Plenck procedure of removing the antral mucosa and prepyloric closure of the seromuscular layers, or a vagotomy and gastro-enterostomy may be performed instead. (Pancreatitis has, however, been reported even after simple gastro-enterostomy.) In cases of gastric ulcers penetrating the pancreas the stomach should

Table I.—CASES OF POST-GASTRECTOMY PANCREATITIS TREATED BETWEEN 1944 AND 1958 AT ST. JAMES'S HOSPITAL, BALHAM

NAME	AGE AND SEX	TYPE OF GASTRECTOMY	ONSET OF PANCREATITIS	RESULT	PRESUMED CAUSE	COMMENT
G. L.	42 M.	'Valved Polya' for duodenal ulcer	14 d.	Recovered	? reflux of duodenal content into pancreatic duct	Radiograph showed calcified pancreas 5 yr. later
S. E.	85 F.	Palliative 'valved Polya' for cancer	9 mth.	Recovered	? ditto	Diagnosed clinically and by raised urinary diastase
E. J.	41 M.	Retrocolic 'valved Polya' for gastric ulcer	3 wk.	Recovered	Long afferent loop	Confirmed by operation
J. R.	60 M.	Antecolic 'valved Polya' and splenectomy for duodenal ulcer	1 d.	Recovered	Operative trauma to pancreas	Pancreatitis confirmed at laparotomy
J. K.	57	Conversion of gastrojejunum to Billroth I, and dilatation of sphincter of Oddi for chronically dilated common bile-duct	11 d.	Died	Operative trauma to ectopic pancreas. Dilatation of sphincter of Oddi	Pancreatitis confirmed at laparotomy
C. T.	62 M.	Conversion of Billroth I to antecolic 'valved Polya' for anastomotic ulcer	3 yr.	Recovered	Stones in common bile-duct	Diagnosed clinically with very high serum amylase. Five months later cholecystectomy and sphincterotomy for stones in gall-bladder and common bile-duct. Showed chronic pancreatitis
W. W.	64 M.	Antecolic 'valved Polya' for duodenal ulcer	1 mth. 2 mth. 3 mth.	Recovered	? reflux of duodenal content	Diagnosed clinically
W. C.	38 M.	Antecolic 'valved Polya' for duodenal ulcer	5 yr.	Died	Reflux from obstructed afferent loop	Post-mortem showed grossly dilated duodenum
S. B.	54 M.	'Valved Polya' with a long afferent loop	—	Recovered	? reflux of duodenal content	Chronic pancreatitis discovered at laparotomy 2 yr. later

be 'pinched off' rather than cut off, so as to leave the ulcer bed in situ in the pancreas. If a carcinoma of the stomach invades the pancreas partial pancreatectomy is performed, removing the growth in continuity with the stomach. This is not only more radical, but much safer than shaving off parts of the anterior surface of the pancreas (merely stripping the peritoneum from the anterior surface of the gland in a carcinoma case is safe, however). It is unnecessary to cannulate the common bile-ducts even in a difficult gastrectomy provided that dissection is kept close to the duodenal wall.

As acute or chronic afferent loop distension is a probable causative agent in some cases, a technique which avoids this complication should be used. In practice this means that if in a gastro-jejunal reconstruction the afferent loop is united to the lesser curve of the stomach, the length from duodenojejunal flexure to lesser curve should be kept to a minimum, only 3–4 in. even in an antecolic anastomosis (Tanner, 1953).

Cases of post-operative pancreatitis are best managed conservatively provided a confident diagnosis can be made. Intravenous saline and glucose drips, gastric suction, and antibiotics are used, and a careful watch is kept on the urinary output. Drugs such as morphine and codeine may cause spasm of the sphincter of Oddi and are best avoided and pethidine used instead. In severe shock, cortisone and ACTH may help to tide the patient over a difficult phase. Noradrenaline should be used as moderately as possible for severe hypotension, and combined with intranasal oxygen to combat cerebral anoxia.

If there is doubt as to the diagnosis, or if there is no response to medical management, the abdomen should be re-explored to exclude other lesions.

If pancreatitis is confirmed, any peritoneal exudate is aspirated and a drain inserted into retroperitoneal boggy areas near the pancreas. Pancreatic juice may escape from this region, and will need the customary precautions to prevent skin excoriation.

A careful study of the afferent loop should be made. If it is grossly dilated, inflamed, or if its wall shows signs of recent exudation or adhesion, then persistent or recurrent afferent loop obstruction is likely, and a small anastomosis should be made between the efferent and afferent jejunal loops.

SUMMARY

Pancreatitis is a serious complication when it follows gastrectomy. When it occurs it is nearly always after the Polya-type of operation. The incidence in the series here reported (*Table I*) is difficult to give exactly, as 2 of the cases were admitted with the complication from other hospitals. Four cases followed operation by one of the authors, however, and in this case the incidence would be 4 out of a total of 1881 gastrectomies carried out in our hospital between 1944 and 1958 (15 years). Pancreatitis may arise in the early post-operative period or after some weeks or even years.

There are various aetiological factors, of which injury to the pancreas and obstruction of the afferent loop are very important. Damage to the pancreas may be prevented by dissection close to the duodenum, the Bancroft or Plenck procedure, 'pinching off' gastric ulcers, and partial pancreatectomy where a gastric carcinoma is invading the pancreas. Sometimes the afferent loop is found to be distended at operation for post-gastrectomy pancreatitis, in which case a small anastomosis with the efferent loop should be made.

REFERENCES

BURTON, C. C., ECKMAN, W. G., jun., and HAXO, J. (1957), *Amer. J. Surg.*, **94**, 70.
DUNPHY, J. E., BROOKS, J. R., and ACKROYD, F. (1953), *New Engl. J. Med.*, **248**, 445.
HOWELL, C. W., and BERGH, G. S. (1950), *Gastroenterology*, **16**, 309.
MCKENZIE, W. C. (1954), *Ann. R. Coll. Surg.*, **15**, 220.
MAHAFFEY, J. H., and HOWARD, J. M. (1955), *Arch. Surg., Chicago*, **70**, 348.
MILLBOURN, E. (1949), *Acta chir. scand.*, **98**, 1.
POPPER, H. L., and NECHELES, H. (1951), *Surg. Gynec. Obstet.*, **93**, 621.
TANNER, N. C. (1953), *Trans. med. Soc. Lond.*, **70**, 156.

A CASE OF HYDATID CYST OF THE PANCREAS

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HYDATID disease appears to be uncommon in Lewis, as it is in Britain as a whole, 2 cases having been encountered by Jamieson (1955) in 26 years. Dew (1928), quoting Devé, gives the figure of 14 per cent as the proportion of peripheral cysts occurring outside the liver and lung. The same author refers to 5 cases of hydatid cyst of the pancreas. The Hydatid Registry of the Royal College of Surgeons of Australasia only went up to Dec. 12, 1936, and out of 1024 cases recorded only one was situated in the pancreas. Further search of their records by Fitzpatrick (1958) up to 1945 revealed 2 instances of involvement of the pancreas out of 1802 cases of hydatid disease. He pointed out that as the Registry tended to contain the rarer or more complicated cases, the incidence in general is probably smaller than this.

The following case of hydatid cyst of the pancreas occurred in a girl aged 14 years.

CASE REPORT

A. M., a female, aged 14 years, was admitted to this hospital on Feb. 11, 1958, complaining of abdominal pain and vomiting which had been present for three hours.

On June 2, 1955, she had a thoracotomy and right lobectomy for a hydatid cyst in the right lower lobe. Following this operation her convalescence was stormy and at one stage it was noted that she was jaundiced.

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ON EXAMINATION.—The thoracotomy scar was well healed and there were no abnormal signs in the chest. There was a visible rounded swelling in the epigastrium. It was smooth, mobile, and not tender, moving vertically on respiration. It could be manipulated under the costal margin on both sides and transmitted the pulsation of the aorta. No other abnormality was detected and the pain settled quickly. A synchronous gall-bladder visualization and barium meal showed the stomach to be deformed by a rounded swelling occupying the lesser curvature and depressing the duodenum (*Fig.* 162). The gall-bladder functioned well and the common bile-duct showed up with normal outline (*Fig.* 163). Radiograph of the chest showed no abnormality. The diagnosis seemed to be between pancreatic cyst, hydatid cyst, and enterogenous cyst. The normal common bile-duct appeared to rule out a choledochus cyst.

FIG. 162.—Synchronous barium-meal and gall-bladder visualization showing the deformity of the stomach and duodenum. The gall-bladder shadow is also visible.

FIG. 163.—Synchronous gall-bladder visualization and barium meal showing distortion of stomach and duodenum by the cyst. The gall-bladder and common bile-duct are normal in outline.

FIG. 164.—The hydatid cyst re-inflated with formalin. The ligature is on the stump of the 'duct'.

AT OPERATION.—Laparotomy on Feb. 19, 1958, disclosed a cystic tumour occupying the region of the lesser curvature of the stomach. The lesser sac was opened above and below the stomach, and the cyst, about the size of an orange, was found to arise from the head of the pancreas. During quite gentle manipulation the cyst emptied readily without intraperitoneal leakage. No other abnormality was found in the abdomen. The cyst was dissected free, taking the adventitious layer, as at that stage the diagnosis was still in doubt. On the deep aspect a duct-like structure presented which was of the thickness and calibre of the long saphenous vein at the ankle. Through a small nick in its wall a probe ran well into the head of the pancreas, but could not be guided into the duodenum. After removal the cyst was re-inflated with formalin through the 'duct' (*Fig.* 164). The cyst bisected with a ligature round the stump of the 'duct' is shown in *Fig.* 165. The true wall of the cyst has partially collapsed and separated from the adventitious layer.

Histological examination showed a hydatid cyst adherent to pancreatic tissue. The true wall showed the characteristic lamination (*Fig.* 166). A few hydatid scolices were present (*Fig.* 167).

The patient's convalescence was uncomplicated and she was discharged on her twelfth post-operative day.

PROGRESS.—The patient remains well and free from symptoms or signs. The hydatid complement-fixation test shows a falling titre, being positive: 1 in 128 on

April 14, 1958; 1 in 64 on July 8, 1958; 1 in 8 on Jan. 13, 1959.

Bensted and Atkinson (1953) presented evidence to show that after excision of the primary cyst the complement-fixation titre tends to fall slowly but will rise again if further cysts develop. The present falling titre is therefore no guarantee that a secondary cyst will not appear.

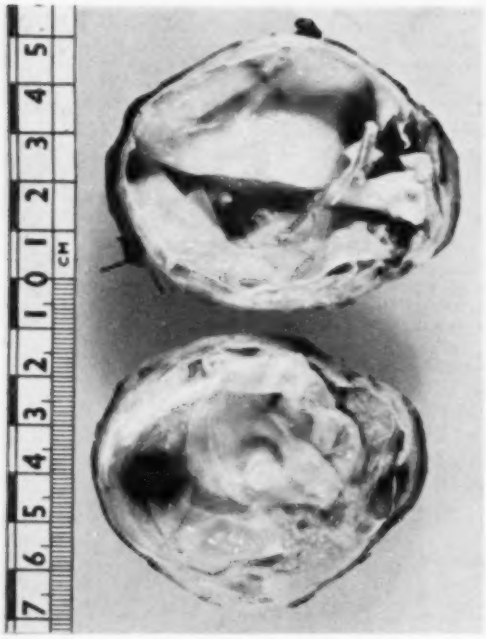

FIG. 165.—The hydatid cyst bisected. The true wall has partially collapsed and separated from the adventitious layer.

SUMMARY

A case of hydatid cyst of the pancreas is described. The cyst communicated with the pancreatic duct and leaked along it during operation. The cyst is presumed to be of the same age as the pulmonary one. In this connexion the jaundice during convalescence following lobectomy may be significant. It is unusual for a hydatid to become apparent at such an early age.

Acknowledgements.—Our thanks are due to Mr. P. L. Brunnen, Aberdeen, for details of the operation for the lung hydatid; Mr. Fitzpatrick, Hamilton, Australia, for information from the Australian Hydatid Registry; Dr. H. J. R. Kirkpatrick and Mr. W. Rose, Inverness, for the histological report and photomicrographs; Dr. H. Williams, Inverness, for the complement-fixation results; Mr. C. E. L. Hunt, Inverness, and Mr. Gabriel Donald, Glasgow, for the photographs.

FIG. 166.—Photomicrograph of the true wall of the cyst showing the characteristic lamination. (× 150.)

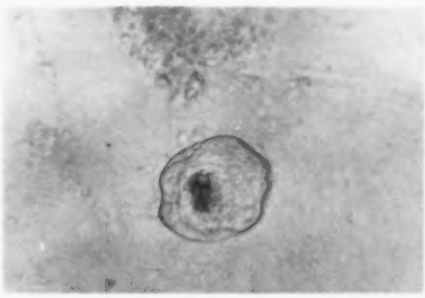

FIG. 167.—Photomicrograph of scolex in unstained preparation of cyst fluid. (× 200.)

REFERENCES

BENSTED, H. J., and ATKINSON, J. D. (1953), *Lancet*, **1**, 365.
DEW, H. R. (1928), *Hydatid Disease*. Sydney: Australian Medical Publications.
FITZPATRICK, S. C. (1958), personal communication.
JAMIESON, E. N. (1955), personal communication.

ISOLATED INJURY OF THE PANCREAS FROM NON-PENETRATING ABDOMINAL TRAUMA

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THE pancreas is so well protected from non-penetrating trauma that it is affected in less than 1 per cent of all closed abdominal injuries (Clarke, 1954; Allen and Curry, 1957) and is seldom damaged even by severe crushing. On occasion, however, it alone is involved, and these cases of isolated injury seem to fall into a special category. The causative blow is often slight in proportion to the glandular injury, which varies from a localized contusion to complete transverse rupture, and symptoms are typically slow to appear and deceptively mild. Many of the minor degrees of injury undoubtedly escape recognition because they never come to laparotomy, and others are diagnosed only in retrospect when a pseudocyst makes its appearance; but complete rupture is a serious injury that ends fatally if operation is too long delayed. Fortunately it is rare. It was first described in association with other visceral injuries by Travers in 1827, but the first example of complete rupture as an isolated lesion occurring after non-penetrating trauma was reported by Jaun (1856) and only 19 others have been recorded since (*Table I*).

Two cases are reported here. One is the twenty-first example of a complete rupture, successfully treated by immediate resection of the distal fragment —a method hitherto seldom used. In the second case, in addition to some of the better-known complications, duodenal obstruction added to the difficulties. Together these cases illustrate many of the problems of diagnosis and treatment of these rare and remarkable injuries.

CASE REPORTS

Case 1.—**Complete transverse rupture—immediate distal pancreatectomy—uneventful recovery.**

P. M., a man aged 22 years, was kicked in the belly a few minutes before the end of a game of football. He was not winded, and after a moment of intense pain was able to walk off the field, wash, change, and make his own way home. Three hours later he walked into King George V Hospital, Ilford, complaining of abdominal discomfort.

ON EXAMINATION.—At 7 p.m., no bruising could be found, and in the abdomen, which moved well with respiration, there was neither tenderness nor guarding, and bowel-sounds were clearly heard. Rectal examination was normal. He was kept under observation and after an hour the only significant change in his condition was the disappearance of bowel-sounds. At this time his pulse-rate was 80 per minute and his blood-pressure 120/80 mm. Hg. Though feeling well he still had a dull ache in the pit of the stomach radiating to the back.

A catheter passed at 8.30 p.m. withdrew 5 oz. of clear amber urine containing a trace of reducing substance, the significance of which was not then appreciated. Radiographs of the abdomen were normal. He was repeatedly examined in the next two hours, but there was no change in his condition until 11 p.m., when he complained of some discomfort in the right shoulder, and for the first time was found to be slightly tender in the epigastrium. There were no signs of intraperitoneal fluid, bowel-sounds were still inaudible, and the pulse-rate and the blood-pressure were unchanged. As the symptoms persisted surgical exploration was indicated and was undertaken eleven hours after the injury.

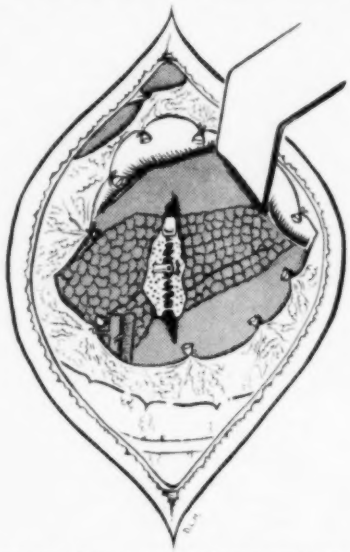

FIG. 168.—*Case* 1. Drawing showing tear in the pancreas, with the surfaces of the fragments about half an inch apart, and the severed pancreatic duct protruding.

AT OPERATION.—Under general anæsthesia (Dr. Derek Leede) a midline epigastric incision was made. The peritoneal cavity was full of dark blood, the source of which could not be seen. The liver was intact. A very large quantity of blood was dislodged when the spleen was palpated, and an irregularity on its lateral surface was taken to be a laceration, but when the spleen had been removed this was seen to be a deep developmental fissure.

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The lesser sac was opened through the gastrocolic omentum and about half a pint of clotted blood removed. The pancreas was then seen to have been torn in half by a sagittal rent directly overlying the spine. The raw and discoloured surfaces of the fragments lay about half an inch apart, and from the right side there protruded about half an inch of severed pancreatic duct (*Fig.* 168). The part of the pancreas to the left of the tear was dissected out without difficulty. The pancreatic duct was ligated, and the stump of the gland sutured with interrupted mattress sutures of thread.

The other viscera were found to be intact. There was a large retroperitoneal hæmatoma overlying the left kidney, tracking behind the descending colon, which did not call for special treatment.

A sump drain was led from the pancreatic bed through a separate stab wound, and the abdomen was closed in layers with nylon. A careful estimate of the amount of blood and blood-clot removed from the peritoneal cavity showed that about five pints had been lost; three of these were replaced during the operation and two more in the next eight hours.

On return to the ward continuous suction was applied to the central catheter of the sump drain. The patient's general condition at all times was good. Bowel-sounds were heard after fourteen hours and flatus was passed after thirty.

For the first three post-operative days the patient was moody, resentful, and complaining—quite different from his normal personality, as we came to know it later on. This aberration was probably significant, for similar mental changes have been remarked in other cases of pancreatic injury. It is not explained by changes in blood-chemistry for this was virtually normal: blood-sugar 116 mg./100 ml., serum potassium 4·3 mEq./l., sodium 156 mEq./l., chloride 77 mEq./l. as NaCl, urea 30 mg./100 ml. His urinary diastase was also within normal limits—33·3 units. During these three days he was disinclined to cough and had to have a bronchoscopy on the third post-operative day for collapse of the left lower lobe. From then on his improvement was uninterrupted.

Between 5 and 10 ml. of clear fluid, containing no active trypsin, and with a diastatic activity of less than 20 units, were aspirated from the sump drain on each of the first three days after operation. The drain was removed on the seventh day and its track remained dry thereafter. The patient was discharged symptom-free on the eighteenth day after operation with a normal serum

Table I.—ISOLATED COMPLETE RUPTURES OF THE PANCREAS

CASE	AUTHOR	DATE	SEX	AGE	INJURY	OPERATION	REMARKS
1	Jaun	1856	M.	50	Assaulted and kicked. Fainted. Later rose and walked home	—	Death after 18 hr.
2	Wilks and Moxon	1875	M.	16	Crushed	—	Died
3	Wagstaff	1895	M.	—	Fell off cart. Also fractured shaft of femur	—	Death on 4th d.
4	Villière	1895	M.	20	Crushed	Laparotomy	Died next d.
5	St. Bart's Museum	1897	M.	37	Crushed between vans. Collapsed 3rd d.	—	Died 3rd d.
6	Stern	1899	M.	37	Crushed	Laparotomy after 3 wk.	Died 5th d.
7	Simmonds	1902	M.	51	Run over	—	Died 5th d.
8	Von Schneider	1904	M.	18	Crushed	Laparotomy 64 hr.	Died 2nd d.
9	Garré	1905	M.	24	Crushed	Sutured	Lived. Fistula 3 wk.
10	Heineke	1907	M.	14	Crushed	Sutured	Lived. Fistula 4 mth.
11	Newton	1929	M.	30	Crushed	Sutured	Lived. Fistula 3 wk.
12	Fast	1930	F.	20	Motor-car accident. Pseudocyst on 8th d.	Laparotomy 8th d.	Lived. Fistula 3 wk.
13	Venable	1932	M.	56	Crushed	Laparotomy and drainage after 6 hr.	Died
14	Brown and Barlow	1932	M.	44	Run over	Laparotomy at 5 hr.	Lived. Fistula 5 mth.
15	Curr	1944	M.	20	Crushed	Laparotomy 6th hr. Sutured and packed	Lived. Fistula 9 wk.
16	Burnett	1955	M.	20	Blow on abdomen at football	Laparotomy 30th hr. Sutured	Lived. Fistula 5 wk.
17	Kinnaird	1956	M.	21	Crushed	Distal pancreatectomy. Initial recovery	Died. Secondary hæmorrhage 8th d.
18	Hannon and Sprafka	1957	F.	32	Beaten by husband	Distal pancreatectomy after 56 hr.	Lived. Uneventful recovery without any fistula
19			M.	3	Motor-car accident	Distal pancreatectomy after 24 hr.	Lived. Uneventful recovery
20			M.	9	Fell from cycle, struck in abdomen	Distal pancreatectomy after 24 hr.	Lived. Uneventful recovery
21	Blandy, Hamblen and Kerr	1959	M.	22	Kicked in abdomen at football	Distal pancreatectomy after 11 hr.	Lived. Uneventful recovery

diastase and a normal blood-sugar tolerance curve. In four months he was playing football again, and for more than a year has remained perfectly well, without any glycosuria.

Case 2.—**Contusion of head and neck of pancreas—partial pancreatic fistula—duodenal obstruction—duodenojejunostomy and cystogastrostomy.**

C. F., a healthy girl aged 13 years, holiday-making on a farm, fell off a tractor one morning at 10 a.m., and was struck in the epigastrium by an angular projection. She thought nothing of this, and continued at play. Three or four hours later she began to complain of epigastric pain and vomited her luncheon. She was examined then, but no abnormal physical signs were found. As the pain and sickness continued overnight, she was admitted to the

FIG. 169.—*Case* 2. Barium meal showing obstruction at the third part of the duodenum. The cyst, filled with lipiodol the previous day, is still outlined, and in this projection appears in front of the stomach, level with the upper end of the safety pin.

Cumberland Infirmary on the following morning. On admission twenty-four hours after the injury, a small bruise could just be discerned half-way between the xiphisternum and the umbilicus to the right of the midline, with a little tenderness and guarding down the outer border of the rectus sheath. As there were no signs of free fluid, no pyrexia, and nothing abnormal in a radiograph of the abdomen, the patient was kept under observation. Twelve hours later, i.e., thirty-six hours after the injury, her symptoms had become rather more severe and her pulse-rate and temperature had risen slightly. Exploration was decided on.

AT OPERATION.—Under general anæsthesia (Dr. D. Hunter Smith) the abdomen was opened through a right paramedian incision. A considerable quantity of blood-stained free fluid was found in the peritoneal cavity and patches of fat necrosis were seen in the greater omentum and in the gastro-hepatic and gastrocolic omenta.

The pancreas was exposed. There was a diffuse subcapsular hæmatoma of the head and neck but no laceration. The body and tail were normal. After mobilizing its second part, the whole of the duodenum was examined and found to be intact, as were the other viscera.

After leading a drain through a separate stab wound in the right flank the incision was closed with unabsorbable sutures.

POST-OPERATIVE PROGRESS.—Initially, all went well and the drain was removed on the fourth day. On the sixth day the pulse-rate and temperature rose, and the patient began to have stabbing pains in the right flank which increased until on the twelfth day the drainage wound re-opened and discharged a quantity of watery fluid, with relief of her pain. For the next few days there was a profuse discharge of pancreatic fluid unmixed with bile or bowel contents, and the skin became excoriated for 3 in. around the fistula. Gradually the discharge lessened, and ceased altogether on the twenty-third day, but fluid then collected subcutaneously in the flank and the patient began to vomit. The stenosed fistulous track had to be reopened. For a week after this she was comparatively well, but on the thirty-first post-operative day she began to vomit again, and required intravenous replacement of her fluid and electrolyte deficiency. A sinogram that day, and a barium meal on the next, showed that the fistula originated from a small cyst in the neck of the pancreas, and that there was complete obstruction of the third part of the duodenum (*Fig.* 169).

SECOND OPERATION (thirty-third post-operative day).—Under general anæsthesia (Dr. R. L. McMillan) the abdomen was re-opened. Retroperitoneal exudate had permeated the upper part of the root of the mesentery, and an indurated mass was producing obstruction where the superior mesenteric vessels crossed the third part of the duodenum.

The obstruction was relieved by a side-to-side anastomosis between the dilated third part of the duodenum and the proximal jejunum. The track of the fistula was divided flush with the surface of the pancreas leaving a hole, about one-third of an inch in diameter, for anastomosis with the adjacent pyloric antrum. A drain was led from this cystogastrostomy and the incision closed with unabsorbable sutures.

Convalescence this time was swift and uneventful. In ten days the patient's wounds were healed and her appetite was enormous. She went home on the twelfth day—the forty-sixth after her accident—and in the ensuing fortnight had only one episode of abdominal pain. This lasted two hours and was attributed by the patient to a surfeit of strawberries. A barium meal four weeks after the second operation did not outline the cyst. It showed that the anastomosis between the still slightly dilated third part of the duodenum and the jejunum was working well, and that obstruction to the duodenum beyond this point was still complete.

Two years afterwards the girl's mother wrote to say that her daughter was very well, and living a normal life, without pain, nausea, or vomiting, or impairment of appetite.

PATHOLOGY

How the pancreas can be severed while all the other viscera escape injury has been the subject of much speculation. In more than half of the recorded cases of complete rupture the abdomen had been run over or crushed, and the pancreas could well have been ground against the spine, but in both our cases, as in many others, the cause of the injury was a blow on the abdomen that hardly seemed severe enough to cause the injury that was found. Perhaps here the abdominal muscles were caught off guard and the pancreas momentarily forced up against the spine

(Aldis, 1946); perhaps the singular vulnerability of the pancreas is due to contrecoup (Venable, 1932). Neither explanation is wholly convincing.

If the rupture is complete the main pancreatic duct is torn, as well as one or more substantial vessels coursing transversely through the substance of the pancreas (Falconer and Griffith, 1950) so that blood and pancreatic juice enter the peritoneal cavity. In some cases hæmorrhage causes death within hours; in others there is little bleeding, but unless operated on promptly, the patient dies after several days (Jaun, 1856, the St. Bartholomew's Hospital Museum case), though on one occasion a cyst is known to have formed (Fast, 1930).

Slighter lesions like contusion tend to enlarge, as enzymes, set free from damaged pancreatic cells and ductules, digest the hæmatoma, encourage further bleeding, and erode larger ducts (Aldis, 1946; Cattell and Warren, 1953). Pancreatic necrosis, brought about largely by liberation of intracellular enzymes (Reid, Paulette, Challis, and Hinton, 1958), may be extensive. The products of autolysis and digestion provoke an intense inflammatory reaction with the result that fibrous tissue surrounds and circumscribes the fluid wherever it tracks, to form a pseudocyst with a dense wall, in the gland itself, or anywhere behind the peritoneum, or in the lesser sac.

Fistulæ.—An external fistula is a troublesome complication of pancreatic injury which commonly follows early operation; it is indeed the purpose of drainage to provide an outlet for collections of fluid. At a later stage in the disease, the creation of a fistula by external drainage of a cyst used to be the standard procedure and still has occasional applications.

A fistula has problems of its own. It is not easy to maintain fluid and electrolyte equilibrium with losses ranging between 800 and 2000 ml. of juice in twenty-four hours (Aldis, 1946; Sinclair, 1956), and depletion quickly leads to pancreatic asthenia, a syndrome characterized by irritability and depression, anorexia, and rapid loss of weight (Lahey and Lium, 1937). Smaller losses from partial fistulæ are easily corrected and nutrition is not impaired, but digestion of the skin may be just as distressing, and stenosis of the track with retention of secretion is just as liable to cause trouble. Both these complications were seen in *Case* 2.

The fistula heals spontaneously if juice secreted distal to the breach in the duct can get to the duodenum, or if the part of the gland producing it is destroyed by necrosis, autolysis, or infection. According to Aldis 80 per cent of fistulæ heal, if given time, most of them taking six to eight weeks.

Intestinal Obstruction from Pancreatitis.—The process which starts with the liberation of pancreatic ferments by trauma, infection, or other means very seldom produces intestinal obstruction, for the pancreas lies behind the peritoneum and most of it is separated from the general peritoneal cavity by the lesser sac. A case of high jejunal obstruction was reported by Moore (1956), who found two loops of small bowel adhering to an inflammatory mass in the tail of the pancreas, and de Vidas (1947) had a case of obstruction of the ileum by adhesions soon after acute hæmorrhagic necrosis. Large-bowel obstruction is rather less rare, and occurs at the splenic flexure, where the colon is fixed to the posterior abdominal wall and liable to envelopment by retroperitoneal exudates. Miln and Barclay (1952) reported 2 cases of colonic obstruction in acute pancreatitis, and Remington, Mayo, and Dockerty (1947) 2 cases of subacute obstruction in pancreatic disease of longer standing.

Pancreatitis is frequently mentioned as a cause of duodenal obstruction, but reports of cases are hard to find. Comfort, Gambill, and Baggenstoss (1946) had a case of pancreatitis which developed duodenal obstruction and gastric dilatation, but the cause was not exposed at operation. McGrigor (1953) found infected cysts in the head of the gland compressing the first and second parts of the duodenum. Two other cases (Cattell and Warren, 1953; Kinnaird, 1956) bear a closer resemblance to the one reported here although the actual site of obstruction was different, involving, in Kinnaird's case, not the duodenum but the distal part of the stomach. In each of these cases the injury to the pancreas was complicated by a fistula, and this was followed after a few weeks by the development of obstruction, which needed urgent operation for its relief.

DIAGNOSIS

Some early authors wrote that severe shock and collapse were typical of pancreatic injury, and others remarked on the intensity of the abdominal pain (Leith, 1895; Mikulicz-Radecki, 1903). Stern (1930) and Venable (1932) borrowed Moynihan's (1926) account of the unendurable agony of acute pancreatitis to embellish their descriptions of pancreatic injury. Though this may be true of some injuries, most published accounts paint a very different picture, even when the rupture has been complete. Garré (1905) remarked on the absence of shock, the steady pulse-rate, and the good colour of his patient, and Grey Turner (1913) commented on the striking absence of rigidity in both of his cases.

Pain, not necessarily severe, is nevertheless the chief symptom. It is felt mainly in the epigastrium with radiation to the back, or to either flank, and is often accompanied by nausea and vomiting. If the gland is badly damaged it may begin with the injury, but usually there is little or no pain for several hours. Delayed onset and gradual aggravation of symptoms are characteristic of pancreatic injury, and at first the abdominal signs are few and vague. Tenderness and rigidity are inconstant; the disappearance of bowel-sounds—a useful index of deterioration—is not specific. If facilities for its measurement are available, a rise in the concentration of serum amylase may give warning of pancreatic damage (Naffziger and McCorkle, 1943). In so far as the pancreas is concerned, radiography is no help when the injury is recent. In nearly every case the abdomen must be opened on suspicion, for it is well known that there may be severe visceral injury with minimal signs. In the exceptional cases with shock, cyanosis, and dyspnœa, there will be no doubt about the need for laparotomy.

Even with the abdomen laid open, it is easy to overlook a pancreatic injury if the tell-tale fat necrosis has not had time to appear, or if other visceral injuries provide seemingly adequate cause for the pre-operative and operative findings. Just as

necessary as a careful search for concealed duodenal lacerations is a deliberate examination of the pancreas (Moynihan, 1926).

TREATMENT

The simplest life-saving procedure in cases of laceration of the pancreas is the control of hæmorrhage (by under-running the bleeding points) and the provision of drainage. Though a fistula is then inevitable, many authorities recommend no more than this. Effective repair of the duct is impossible, and any attempt at suturing the gland is found to fail in the presence of a leak from a main duct, but if the injury is to the body or tail, the policy advised by Walton (1923), Moynihan (1926), and Aird (1957) of removing the part of the gland to the left of the laceration is well worth consideration. This was the operation carried out in *Case* 1, and the result was gratifying. The dangers and discomforts which attend a fistula were eliminated, and the rapid and relatively trouble-free convalescence contrasts strongly with the stormy course of *Case* 2, where the initial lesion was much less severe.

Immediate distal pancreatectomy is an operation that has seldom been employed and we have found reports of only four other cases. The first was making a satisfactory recovery when sudden and uncontrollable hæmorrhage caused his death on the eighth post-operative day, anticoagulants having been given from the fifth day for a rising platelet count (Kinnaird, 1956). The other three, who recovered without incident, were reported by Hannon and Sprafka (1957).

The many methods of treating pancreatic fistulæ and cysts have been authoritatively discussed in a number of recent publications (Lahey and Lium, 1937; Aldis, 1946; Cattell and Warren, 1953; Sinclair, 1955; Clyne, 1955; Maingot, 1955; Twiss and Oppenheim, 1955; Aird, 1957.) In *Case* 2 the opportunity was taken, at an emergency operation for obstruction, to deal with the fistula which would otherwise have been treated conservatively for a longer period. In this case cystogastrostomy was applicable and easy, and the result has been satisfactory.

Intestinal Obstruction.—If this very rare complication develops, it must be treated according to what is found at operation. Duodenal obstruction is effectively overcome by a short-circuiting operation, but obstruction at the splenic flexure simulates carcinoma, and the prudent course may be to treat it as such. If a definite diagnosis of pancreatitis can be made it is, however, sometimes possible to free the colon from the encircling fibrous tissue.

SUMMARY

1. Isolated pancreatic injuries are rare, but tend to conform to a pattern. The local lesion varies in severity from a slight contusion to complete transverse rupture, of which 20 cases reported in the literature are tabulated and compared.

2. Another case of complete rupture of the body of the pancreas, and one of contusion of the head and neck, are described. Each was caused by a blow on the abdomen, each had the slow onset typical of this injury.

3. The complete rupture was treated by immediate distal pancreatectomy with uneventful recovery. The contusion was drained, and after developing a partial pancreatic fistula, had a complete duodenal obstruction. Cystogastrostomy and duodenojejunostomy at a second operation led to recovery.

4. The peculiar difficulties in the diagnosis and treatment of these rare injuries are discussed with special reference to the hazards of a pancreatic fistula, with emphasis on duodenal obstruction, and the advantages to be gained by immediate distal pancreatectomy when it is feasible.

Acknowledgements.—We are grateful to Mr. Hermon Taylor for his advice in the management of *Case* 1, and for his permission to report it. *Case* 2 was treated under the guidance of Mr. R. M. Hill, and it is a pleasure to acknowledge his help and also his interest in the preparation of this paper. We thank Dr. W. G. Scott-Harden for permission to reproduce the radiograph, and Dr. W. J. Hanbury, Curator of the Pathological Museum, St. Bartholomew's Hospital, for enabling us to examine their unique specimen.

REFERENCES

AIRD, I. (1957), *Companion in Surgical Studies*, 2nd ed. Edinburgh: E. & S. Livingstone.
ALDIS, A. S. (1946), *Brit. J. Surg.*, **33**, 323.
ALLEN, R. B., and CURRY, G. J. (1957), *Amer. J. Surg.*, **93**, 398.
BROWN, O. H., and BARLOW, L. C. (1932), *J. Amer. med. Ass.*, **98**, 1882.
BURNETT, W. (1955), *Brit. med. J.*, **1**, 1455.
CATTELL, R. B., and WARREN, K. W. (1953), *Surgery of the Pancreas*. Philadelphia: W. B. Saunders.
CLARKE, R. (1954), *Lancet*, **2**, 877.
CLYNE, A. J. (1955), *Brit. J. Surg.*, **43**, 180.
COMFORT, M. W., GAMBILL, E. E., and BAGGENSTOSS, A. H. (1946), *Gastroenterology*, **6**, 239, 376.
CURR, J. F. (1944), *Brit. J. Surg.*, **32**, 386.
FALCONER, C. W. A., and GRIFFITH, S. E. (1950), *Brit. J. Surg.*, **37**, 334.
FAST, W. K. (1930), *J. Amer. med. Ass.* **95**, 1668.
GARRÉ, C. (1905), *Beitr. klin. Chir.*, **46**, 233.
HANNON, D. W., and SPRAFKA, J. (1957), *Ann. Surg.*, **146**, 136.
HEINEKE, H. (1907), *Arch. klin. Chir.*, **84**, 1112.
JAUN, S. M. (1856), *Indian Ann. med. Sci.*, **3**, 721.
KINNAIRD, D. W. (1956), *Amer. J. Surg.*, **91**, 552.
LAHEY, F. H., and LIUM, R. (1937), *Surg. Gynec. Obstet.*, **64**, 79.
LEITH, R. F. C. (1895), *Lancet*, **2**, 770.
MCGRIGOR, R. B. (1953), *Brit. J. Surg.*, **41**, 222.
MAINGOT, R. (1955), *Abdominal Operations*, 3rd ed. London: H. K. Lewis.
MIKULICZ-RADECKI, J. VON (1903), *Ann. Surg.*, **38**, 1.
MILN, D. C., and BARCLAY, T. H. C. (1952), *Lancet*, **2**, 168.
MOORE, T. C. (1956), *Arch. Surg., Chicago*, **73**, 977.
MOYNIHAN, B. G. A. (1926), *Abdominal Operations*, 4th ed. Philadelphia: W. B. Saunders.
NAFFZIGER, H. C., and MCCORKLE, H. J. (1943), *Ann. Surg.*, **118**, 594.
NEWTON, A. (1929), *Surg. Gynec. Obstet.*, **48**, 808.
REID, L. C., PAULETTE, R. E., CHALLIS, T. W., and HINTON, J. W. (1958), *Surgery*, **43**, 538.
REMINGTON, J. H., MAYO, C. W., and DOCKERTY, M. B. (1947), *Proc. Mayo Clin.*, **22**, 260.
SCHNEIDER, VON (1904), *Zbl. Chir.*, **31**, 1470.
SIMMONDS (1902), *Dtsch. med. Wschr.*, **28**, 23*V*.
SINCLAIR, I. S. R. (1955), *Brit. J. Surg.*, **42**, 367.

SINCLAIR, I. S. R. (1956), *Brit. J. Surg.*, **44**, 250.
STERN, E. (1899), *Virchr. gerichtl. Med.*, **18**, 275.
STERN, E. L. (1930), *Amer. J. Surg.*, **8**, 58.
TRAVERS, B. (1827) *Lancet*, **12**, 384.
TURNER, G. GREY (1913), *Brit. J. Surg.*, **1**, 44.
TWISS, J. R., and OPPENHEIM, E. (1955), *Practical Management of Disorders of the Liver, Pancreas, and Biliary Tract*. London: Kimpton.
VENABLE, C. S. (1932), *Surg. Gynec. Obstet.*, **55**, 652.
VIDAS, J. DE (1947), *Med. J. Aust.*, **2**, 333.
VILLIÈRE, M. (1895), *Bull. Soc. Anat. Paris*, **70**, 241.
WAGSTAFF, E. H. (1895), *Lancet*, **1**, 404.
WALTON, A. J. (1923), *The Surgical Dyspepsias*. London: Arnold.
WILKS, S., and MOXON, W. (1875), *Pathological Anatomy*, 2nd ed. London: J. & A. Churchill.

ISLET-CELL TUMOURS OF THE PANCREAS

BY MERVYN SMITH, ADELAIDE

THE history of the unfolding of knowledge about each of the endocrine glands makes a most interesting study and this is not the less true in the case of the endocrine portion of the pancreas.

Although in 1869 the medical student Langerhans had described the histological appearance of islands of tissue in the pancreas differing from the acinar arrangement of the rest of the gland, it had not excited great interest. It was left to Laguesse in 1893 to suggest that this tissue might have an endocrine function, and it was he who named the tissue for the original discoverer. Meanwhile, in 1891, Neve had described an adenoma of the pancreas discovered at autopsy, and later Nicholls (1902), in reporting another tumour, drew attention to its resemblance to normal islet tissue. He named the tumours 'islet-cell pancreatic adenomata', and his report was followed by others over the next twenty years. They were pathological curiosities.

In 1922 Banting and Best discovered insulin and confirmed that hyposecretion of the islet tissue was the cause of diabetes mellitus. Clinical states due to hyposecretion in other endocrine glands such as the pituitary, suprarenal, and thyroid were well known at this time, as were the opposite states of over-secretion of these glands. It was Seale Harris who postulated such a condition as the reverse of diabetes mellitus in 1924, and it is perhaps interesting to hear Harris himself on his thoughts at this time: "One morning after going the rounds with Dr. Banting in the diabetic wards of the Toronto General Hospital, in discussing insulin reactions, I said to him, 'Since you have proved that diabetes is due to deficient secretion of insulin by the pancreas, it seems there should be the opposite condition, in which the pancreas secretes too much insulin, and if so, the spontaneous excessive secretion of insulin in an individual should produce the same symptoms observed in diabetes from overdoses of insulin. Furthermore I am sure that I have seen patients who did not have diabetes and had not used insulin, who have had the same symptoms that we have observed in diabetes from overdoses of insulin.' "

Harris investigated 5 cases in which symptoms similar to overdosage of insulin occurred, and he found that these symptoms were brought on by the fasting state and were associated with a subnormal blood-sugar (below 70 mg. per cent). To show that this was not due to mere fasting, he demonstrated normal blood-sugar levels in 3 cases of malignancy of the upper gastro-intestinal tract, all of whom were literally starving to death (Harris, 1924).

This concept of Harris's was finally established by Wilder and associates, who had a patient with spontaneous hypoglycæmia explored by W. J. Mayo in 1927. The patient was a doctor, aged 40 years, found to have a carcinoma of the islet tissue with metastases, and he died a few weeks after operation (Wilder, Allan, Power, and Robertson, 1927).

It is fitting that the first successful operation for hyperinsulinism should have been carried out in Toronto, where Roscoe Graham in 1929 excised an islet-cell adenoma (Howland, Campbell, Maltby, and Robinson, 1929). Insulin was recovered from the adenoma, which on section looked to be a carcinoma but which had no metastases.

From time to time since then cases have been reported in fairly considerable numbers, mostly from America, so that by 1950 Howard, Moss, and Rhoads, in an excellent article, were able to review no less than 398 cases from the literature.

The seeing of 3 cases, having in all five islet-cell tumours, within a period of 18 months is considered worthy of reporting, enabling some points about the surgery of this condition to be emphasized, and indicating that the condition may be more common than we have perhaps thought in the past.

CASE REPORTS

Case 1.—Mrs. R. D. was a 58-year-old widow who had been subject over the previous two years to attacks in which she would become confused, failing to recognize her relatives, would tend to lose her balance, her speech would become slurred, and her behaviour queer. The onset was always gradual, with symptoms becoming progressively worse until she was staring into space quite confused, this state lasting for several hours. The attacks occurred in the morning or in the late afternoon. Investigations carried out by her physician revealed a normal radiograph of the skull, normal cerebrospinal fluid, negative blood and C.S.F. Wassermann reactions. The electro-encephelogram was normal. A fasting blood-sugar taken during an attack was 32 mg. per cent, while a glucose-tolerance test performed later showed characteristically low readings throughout (*Fig.* 170).

Laparotomy was performed on June 21, 1956. At about the junction of the neck and body of the pancreas, a nodule was felt from the anterior aspect, feeling firmer than the rest of the gland. The peritoneum along the inferior border of the body and tail was divided and this portion of the gland palpated bidigitally, but without feeling any further nodules. The tumour felt was removed

by sharp dissection, as it showed no tendency to shell out. When the pancreas over it had been incised, the tumour was seen to be plum-coloured and was approximately 1½ cm. in diameter. It was reported by Professor J. Robertson as consistent with an insulin-secreting islet-cell tumour (Nesidioblastoma).

On the fifth day the fasting blood-sugar was 113 mg. per cent and on the thirtieth day 110 mg. per cent.

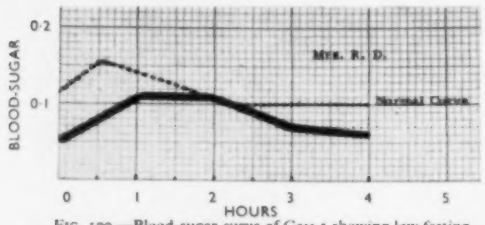

FIG. 170.—Blood-sugar curve of *Case* 1 showing low fasting blood-sugar, low peak figure, falling away steeply in the third and fourth hours.

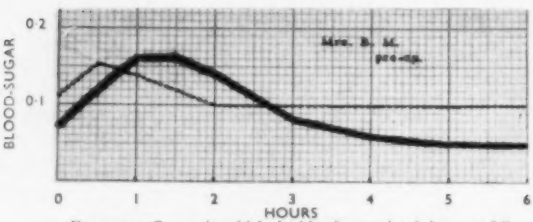

FIG. 171.—*Case* 2, in which the blood-sugar level does not fall below the normal until nearly three hours have elapsed.

Although the site of removal of the tumour had been drained, the drain was removed prematurely and a collection subsequently formed, so that on July 7 a pseudo-pancreatic cyst needed to be drained of 26 oz. of turbid fluid and sump suction instituted for several days.

Convalescence from thenceforth was uneventful although slow, and when last heard from the patient had remained well and free from further attacks.

Case 2.—Mrs. B. M., a married woman of 49 years, was seen by her doctor on March 22, 1957, at 2 p.m. as she had not woken up properly at all that morning. She had gone to bed at 9.30 p.m. the previous night, feeling rather tired. In the morning, instead of waking up, she just lay in bed grunting and taking little or no notice of what was happening. She did not appear to be in pain but just lay apathetically in bed incapable of making any intelligible remark except "I don't know". There was a history of one previous similar attack a month before, but she had recovered after two hours. Nothing significant was found on examination apart from the strange manner, blank look, etc. Her general practitioner, recognizing the possible nature of her trouble, gave her 40 c.c. of 50 per cent glucose solution intravenously with dramatic effect, the patient within 5 minutes conversing normally. A glucose-tolerance test, however, showed a fasting blood-sugar of 82 and a mild diabetic curve. This was later repeated, prolonging the investigation for 6 hours and the result, shown in *Fig.* 171, emphasizes the necessity of making the estimations over a longer period than the 2 hours often taken as the standard. In this case it was 5 hours before the blood-sugar had fallen to 50. On these findings, exploration was carried out on May 28 by Mr. Alan Britten-Jones. On full exposure of the pancreas there was revealed a reddish-purple nodule at the junction of the body and tail. This was dissected free with a portion of the surrounding pancreas. The wound was drained. An intravenous infusion of 4 per cent dextrose in *N*/5 saline was given that evening, and a blood-sugar taken post-operatively was 190 mg. per cent. Apart from some thick purulent discharge from the tube, convalescence was satisfactory and the patient was discharged home on June 8, eleven days after operation, and has been free of attacks since. The pathological report by Dr. McLaughlin was of a typical functioning islet-cell tumour of the pancreas. Cells were said closely to resemble normal islet-cells, being ovoid or spherical, with well-defined nuclei and rich in thin-walled capillaries. The tumour was limited by a capsule (*Fig.* 172).

The day following operation the blood-sugar was 150 mg. per cent, the next day it was 140 mg. per cent, and the third post-operative day 160 mg. per cent.

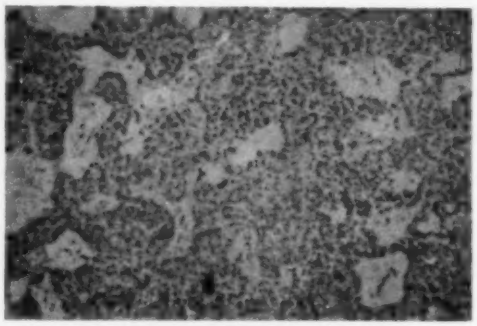

FIG. 172.—Low-power section of tumour from *Case* 2.

Case 3.—Mrs. E. M., a married woman of 43 years, had been well until 12 months previously, when she began having 'turns'. These at first were liable to occur at any hour of the day, varied from a few minutes to several hours, and usually came on without any warning. Her husband said that in a 'turn' she would develop a vacant look about the face, her hands would tremble, and she would not be aware of what was happening to her. She had occasionally fallen over during an attack and had been told that she sometimes became violent when restrained. She sometimes wakened with a headache after the attack.

When she was seen by a physician she was in a poor state of mental health, intelligence tests being performed very badly. She had bilateral plantar extensor responses. At this time it was thought that she had a moderate organic dementia with epilepsy.

Investigations were full, and included an electro-encephalogram, radiography of skull, air encephalogram, cerebrospinal fluid examination, and Wassermann reactions of blood and C.S.F. All were normal. On later questioning it was learned that more recently her attacks had occurred mostly at night and in the early morning, and that if her meals were delayed for any length of time she began to feel trembly and "a bit funny". A glucose-tolerance test was then done (*Fig.* 173) and on this a diagnosis of islet-cell tumour made and the case referred for surgery. It will be noted that the blood-sugar did not fall to 50 until the full four hours had elapsed, while in a further hour it had fallen to 40.

Exploration was carried out on Nov. 19, 1957, after intravenous infusion of 1 litre of 5 per cent dextrose to which an extra 50 g. of glucose had been added. The body and tail of the gland having been mobilized, a small nodule was felt in the tail and removed by sharp dissection. The head of the gland was then mobilized by division of the peritoneum on the lateral aspect of the second part of the duodenum, until the substance of the head could be felt bidigitally (*Fig.* 174). By this method a much larger nodule approximately 2·5 cm. in diameter was felt, and it was able to be shelled out (*Fig.* 175). A

large sump-type drain was inserted and the wound closed. Blood-sugars taken every few hours post-operatively showed levels in the region of 200 mg. per cent, while the urine showed varying amounts of sugar, and insulin was required to be given to control the level through the first night. Convalescence was satisfactory, although there was a slight discharge from the wound after the removal of the tube. A glucose-tolerance test performed on Dec. 3 was considered normal, although in fact it was a low curve and had not been prolonged for the 4-6 hours (*Fig.* 176). She was discharged on Dec. 6. Section of

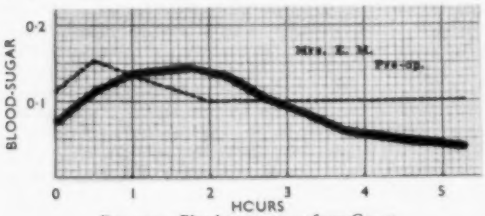

FIG. 173.—Blood-sugar curve from *Case* 3.

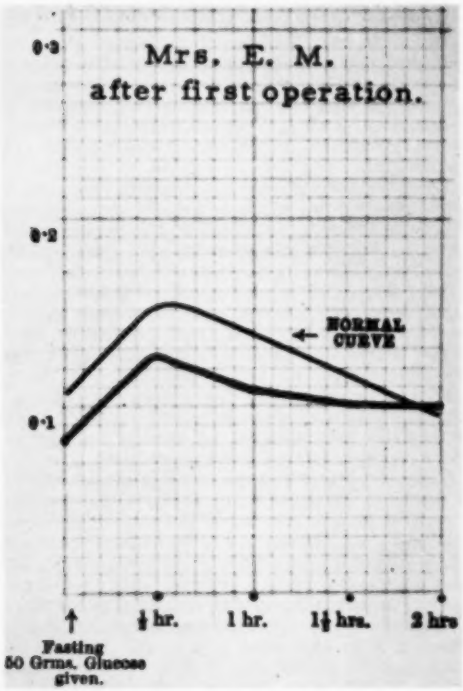

FIG. 176.—Blood-sugar curve of *Case* 3 after the first operation.

both nodules showed them to be islet-cell tumours, with much fibrosis.

One week after discharge she had a typical attack which responded to glucose, and over the ensuing three weeks several more 'turns'. A fasting blood-sugar on Jan. 3, 1958, was 50 mg. per cent and she was therefore re-admitted on Jan. 6 and next day was re-explored. The old wound was incised and the pancreas approached from the tail aspect by mobilizing the spleen and delivering that organ to display the extremity of the pancreas. It was thought that it would be necessarry to excise a large portion of the gland, but in the process of mobilization of the tail a further tumour about 1½ cm. in diameter was found on the posterior aspect of the tail. With no other nodules palpable and this being a distinct tumour, it was excised, and the planned resection abandoned. Frozen section

FIG. 174.—Exposure during dissection of tumour from *Case* 3. The duodenum is seen on the left with the fingers behind it easing it forwards. The adenoma is identifiable in the illustration by the black spot on its surface.

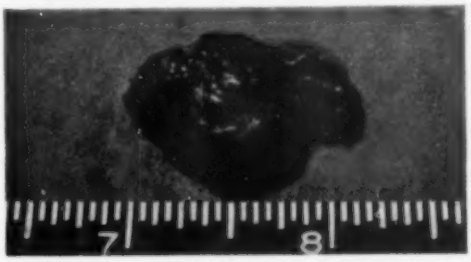

FIG. 175.—Adenoma from *Case* 3.

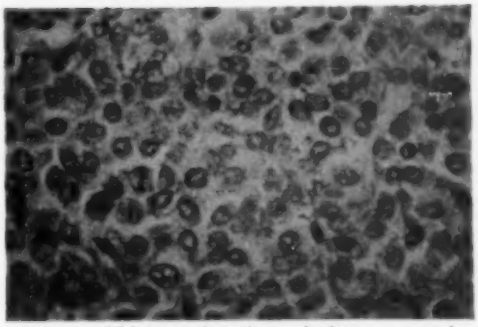

FIG. 177.—High-power photomicrograph of tumour removed from *Case* 3 at the second operation.

confirmed the diagnosis of an islet-cell tumour (*Fig.* 177), and the post-operative course proceeded much as before, with maintenance of blood-sugar levels of approximately 200 mg. per cent for ten hours despite having no glucose intake. Insulin was again required to control this post-operative hyperglycæmia. A blood-sugar curve on Jan. 17 before discharge was normal.

She has been seen from time to time since then, remaining well and free from further attacks. Her intelligence tests are now normal, and it is interesting to note that her plantar responses have become flexor.

DISCUSSION

Conn and Seltzer (1955) have given a classification of the causes of spontaneous hypoglycæmia.

They divide these causes into Organic, Functional, and Factitious. The factitious group implies the surreptitious administration of insulin and need not be dwelt on further here. The functional causes include functional hyperinsulinism, which is an abnormal response of functionally hyper-reactive cells to a normal insulogenic stimulus, and alimentary functional hyperinsulinism such as may occur after gastrectomy or gastro-enterostomy and which represents the normal response of islet tissue to an abnormal insulogenic stimulus—namely, a very high initial elevation of the blood-sugar level. This high initial elevation comes about by virtue of food issuing directly into small bowel where it meets a large absorptive surface instead of being gradually released from the stomach via the pylorus. In response to the extra stimulus, an abnormal amount of insulin is secreted, which gives rise to the hypoglycæmic state 1½–3 hours after food. It can be mimicked in normal individuals by the administration of glucose via a duodenal tube.

It is with the organic causes of hypoglycæmia that we are largely concerned here—that is, the cases in which an anatomical lesion is present. There may be an hepatic cause, anterior pituitary hypofunction, or adrenocortical dysfunction, but a large proportion of these organic hypoglycæmias will be found to be due to oversecretion of insulin from neoplasms of the islet cells.

Pathology.—The types of pancreatic lesion which may be associated with spontaneous hypoglycæmia include benign adenoma (90 per cent), adenocarcinoma (9·3 per cent), and, more rarely, a diffuse hyperplasia of islet tissue.

The adenomata are usually single entities, but in some 12 per cent of cases occur as multiple lesions, usually as two or three tumours, but sometimes more. They vary considerably in size from 2 mm. to 4 cm., commonly between 0·5 and 1·5 cm. in diameter, and are said to be yellow, greyish-white, or brownish-red (Spencer, 1955). All of the five tumours observed in the cases here described were brownish-red. The tumours are firm in consistency and may occur anywhere in the gland or in ectopic pancreatic tissue.

Microscopically, the adenoma is essentially a very large islet, surrounded by a capsule, with possibly some compression of the surrounding pancreas. The columnar or cuboidal cells, of normal size, are arranged in rosettes or as long ribbons of cells and have a rich blood-supply. Fibrosis, hyaline degeneration, or calcification may be seen, just as these changes may be seen in normal islet tissue (Laidlaw, 1938).

Between the benign adenoma group and the malignant tumours there is another group which most authors refer to as 'suspiciously malignant tumours'.

They are so designated because of their histological appearance of apparent invasion of the capsule or of blood-vessels by tumour cells. However, they appear to be malignant in histological appearance only, for such cases as have been traced have invariably followed a benign course.

Of the malignant tumours, which do unquestionably occur, the criterion for diagnosis seems to be the demonstration of metastases, for otherwise the histological appearance is very like that seen in the above group. They have a gloomy prognosis, only 1 case of 37 reviewed by Howard and others (1950) being alive four years after diagnosis.

Diffuse hypertrophy of islet tissue is much rarer than the adenoma group, which is fortunate, as the outlook after resection is poor compared with the good results after excision of an adenoma.

Clinical Features.—The onset is usually insidious, often occurring in middle age, and consists of recurrent attacks of fainting or odd behaviour which can usually be correlated with the need for food. The classical time for these attacks to occur is before breakfast, and many patients have made the discovery for themselves that eating sugar in some form helps them. Indeed, this very fact makes for much of the difficulty in subsequent surgical exploration, as extreme degrees of obesity may be reached by this excessive intake of carbohydrate. It is the periodicity of the attack, whatever the actual symptoms, which gives the lead to the diagnosis, for the symptoms may be very varied and related either to the central nervous system, leading to anxiety, restlessness, disturbance of speech or vision, convulsions, or coma, or to the autonomic system, exhibiting nausea, sweating, palpitations, tachycardia, hot flushes, etc.

Often the same type of attack will be produced by a particular patient, and it is thought likely by some authorities that the *rate* of fall of blood-sugar rather than the absolute blood-sugar level may be the determining factor in the type of attack produced. Thus a slow decline may result in predominantly C.N.S. symptoms, while a rapid fall tends to produce the sweating, vomiting, etc., of autonomic overactivity (Porter and Frantz, 1956). With the symptoms so variable, and often making up a bizarre picture, it is small wonder that these cases often find themselves labelled as neurotic, psychotic, or alcoholic. Indeed it is not uncommon for them to come to surgical treatment via a psychiatrist.

The main consideration in making the diagnosis is having the condition in mind, for once the suspicion of hygoglycæmia is entertained a fasting blood-sugar is indicated, and in the case of an islet-cell tumour will be found to be under 50 mg. per cent. The glucose-tolerance test as a rule will serve to differentiate the functional from the organic types, while, of the organic ones, the absence of symptoms of disease of liver and other organs will indicate the pancreas as the seat of the trouble. The significant finding is the low fasting blood-sugar, and if repeated tests are done this will invariably be found to be well below normal. If not obtained at first it may be necessary to fast the patient for a prolonged period before getting the lowered blood-sugar figure.

The indication for surgical exploration in these cases is the fulfilment of 'Whipple's triad'—attacks of nervous or gastro-intestinal disturbance induced by fasting, these attacks being relieved by the administration of glucose, together with a blood-sugar level below 50 mg. per cent during an attack (Whipple, 1944).

Operation.—The small size of some of these tumours, the granular feel of a normal pancreas, and the fact that the tumour may be situated in the head, body, or tail, makes for some difficulty at operation. In *Cases* 1 and 2 the single adenoma was easily found and removed, but in *Case* 3 difficulty was experienced in finding the two tumours at the first exploration and in fact a third one was missed and only found at re-exploration. Unless the tumour is close to the anterior surface of the gland it cannot be felt except by bidigital palpation. This implies a very thorough mobilization of the gland, first by division of the peritoneum along its inferior border to enable adequate palpation of the body and tail, and, secondly, by mobilization of the second part of the duodenum to enable the head to be examined. If after such adequate palpation no tumour is found, it has been recommended that the body and tail should be resected, on the assumption presumably that generalized hypertrophy is more likely to occur in this half of the gland. That this blind resection is not to be rushed into, however, is well illustrated in the case described by Fisher, Gius, and Janes in 1955.

In this case, with typical symptoms, exploration was carried out but no tumour found. Forty per cent of the pancreas was resected and found to be normal, and symptoms recurred. At the next operation a subtotal pancreatectomy was performed, completing up to a 90 per cent removal. Subsequent recurrence was followed by alloxan therapy and death, and at autopsy an islet-cell tumour was found embedded in the small remaining segment of pancreatic tissue.

An intravenous infusion of glucose is usually started before operation and continued throughout. A sand-bag under the upper lumbar region or the use of the gall-bladder bridge has been found helpful.

The pancreas is conveniently approached through a transverse supra-umbilical incision with wide division of the gastrocolic omentum. The whole of the anterior surface of the gland is then inspected by sight and touch and if a nodule is seen or palpated it is removed. In view of the frequency of multiple tumours, and also of the difficulty of re-exploration in these cases, it is desirable to mobilize the body and tail and the head in turn, as described, to enable bidigital palpation for further tumours, which are then enucleated.

If no tumour is found on first palpation or after mobilization of the gland, then it is recommended that the left half of the gland be resected. This manœuvre is probably made a little easier by removal of the spleen at the same time, and the pancreas is resected up to the superior mesenteric vessels.

It is desirable to drain the lesser sac, and this is best done through a large rubber tube and some form of suction, the tube being shortened only after several days. Blood may sometimes be required during and after operation, and intravenous fluids are kept going and varied according to the requirements of the patient, as shown by blood-sugar levels and urinary sugar tests. Insulin may be required in the first 48-hour period.

SUMMARY

1. The history of the subject of pancreatic islet-cell tumours is briefly reviewed.

2. Two personal cases, and a third, that of a senior colleague, are described.

3. Causes of hypoglycæmia are discussed, emphasizing the organic hyperinsulinisms, and describing the pathology of the pancreatic lesion.

4. Clinical features of islet-cell tumours are described, diagnosis being suspected on the history, and confirmed by blood-sugar determinations, prolonging these if necessary for several hours.

5. Successful diagnosis, with the satisfying of Whipple's criteria, is the indication for surgical treatment. This is described, together with pre- and post-operative management.

6. Failure to make the diagnosis will result at best in a continuation of hypoglycæmic attacks, which will almost certainly be considered functional, while it may have even more tragic consequences in the form of incarceration in a mental home, or ending in death in hypoglycæmic coma.

The cases were all seen and diagnosed in the first instance by physicians, and I am grateful to Dr. Mark Bonnin, Dr. M. E. Chinner, and Dr. J. V. Gordon for allowing me access to their case notes; and to Mr. Alan Britten-Jones for similar courtesy regarding his case. Special mention should also be made of Dr. R. Brummitt, the young graduate who diagnosed the second case at the bedside, and instituted appropriate emergency treatment.

REFERENCES

CONN, J. W., and SELTZER, H. S. (1955), *Amer. J. Med.*, **19**, 460.

FISHER, J., GIUS, J. A., and JANES, R. G. (1955), *Arch. Path. (Lab. Med.)*, **60**, 628.

HARRIS, SEALE, quoted by WHIPPLE, A. O. (1952), *Canad. med. Ass. J.*, **66**, 334.

— — (1924), *J. Amer. med. Ass.*, **83**, 729.

HOWARD, J. M., MOSS, N. H., and RHOADS, J. E. (1950), *Surg. Gynec. Obst. (Int. Abst. Surg.)*, **90**, 417.

HOWLAND, G., CAMPBELL, W. R., MALTBY, E. J., and ROBINSON, W. L., (1929) *J. Amer. med. Ass.*, **93**, 674.

LAIDLAW, G. F. (1938), *Amer. J. Path.*, **14**, 125.

NEVE, E. T. (1891), *Lancet*, **2**, 659.

NICHOLLS, A. G. (1902), *J. med. Res.*, **8**, 385.

PORTER, M. R., and FRANTZ, V. K. (1956), *Amer. J. Med.*, **21**, 944.

SPENCER, H. (1955), *J. Path. Bact.*, **69**, 259.

WHIPPLE, A. O. (1944), *Surgery*, **16**, 289.

WILDER, R. M., ALLAN, F. N., POWER, M. H., and ROBERTSON, H. E. (1927), *J. Amer. med. Ass.*, **89**, 348.

PERFORATING RETICULOSARCOMA OF THE JEJUNUM

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Lymphosarcoma of the small intestine is a relatively rare disease. Of the various types, reticulum-cell sarcoma is the least rare (Aird, 1949). Perforation of a reticulosarcoma has in the past been described as an unusual complication, but it occurred in 47 per cent of the 17 cases described by Irvine and Johnstone (1955).

In the busy surgical department of a provincial hospital 2 cases of reticulosarcoma of the small intestine have come under the surgical care of the writer in seven years. Both tumours have been resected and the patients are still alive and well. The detailed history of the first patient seems worth recording.

CASE REPORT

Mr. A. C., aged 41 years, was admitted to hospital on Sept. 8, 1951. For a period of about three months he had complained of epigastric pain occurring 15–30 min.

Fig. 178.—Sarcoma of bowel. A local lymph-node showing invasion by tumour. H. and E. (× 40.)

after meals and sometimes awakening him at night. During the three weeks before admission the pain had been severe enough to confine him to bed. There had been blood in the stools on two occasions only, and the stools were usually well formed and of normal colour. He had not vomited. He had lost 9 lb. in weight in three months. During the Second World War he had been in the Middle East, but had had no previous illnesses of note. Recently the pain had tended to be more severe on the left side and to radiate to the back. On Sept. 8, 1951, at 1 p.m. he developed a sudden severe pain in the left hypochondrium which radiated to the left iliac fossa and left shoulder-tip. On examination the abdomen was guarded and acutely tender on pressure, especially on the left side. Tenderness was also present in the left lumbar region. Rebound tenderness was marked. Liver dullness was absent.

A provisional diagnosis of perforated gastric ulcer was made and laparotomy was performed as an emergency measure. Free fluid was found in the peritoneal cavity. The stomach and duodenum were normal, but part of the upper jejunum, 2–3 ft. in length, was hyperæmic and œdematous, and in this area of the abdomen a localized peritonitis was present. At the apex of the hyperæmic loop a perforation was found and some 6 in. distal to this the bowel was wrapped in omentum and stenosed. In spite of the perforation the proximal jejunum was somewhat distended. The perforation was oversewn and the inflamed segment isolated by side-to-side enteroanastomosis. It was felt that the lesion was probably a regional jejunitis of the Crohn type. An enlarged mesenteric gland and a piece of jejunum at the site of the perforation were removed for histological examination. After operation oral chloromycetin and parenteral penicillin were given. Convalescence was uneventful. The Widal test was performed and the result was consistent with his previous T.A.B. inoculation. The white-cell count on Sept. 27 was 11,000 per c.mm.

The histological report showed the appearances of acute enteritis. No evidence of Crohn's disease or tuberculosis was found in glands or mucosa. The mesenteric gland showed inflammatory reaction only. He was discharged on Oct. 1 and kept under observation in the Out-patient Department. In November he began to complain of left-sided abdominal pain and diarrhœa, with loss of weight. A barium meal and follow-through examination failed to demonstrate any significant lesion of the jejunum. In December he again began to improve. On Dec. 12 the blood findings were: Hb 75 per cent, R.B.C. 3,800,000 per c.mm., W.B.C. 11,500 per c.mm.; film normal.

On Jan. 9, 1952, he was seen at the Out-patient Department and again complained of sickness and diarrhœa, with loss of weight and persistent pain and tenderness on pressure in the left side of the abdomen. He was re-admitted for laparotomy and the following pre-operative investigations performed:—

Blood.—Blood-urea 25 mg. per cent. Serum alkaline phosphatase 7 K.A. units. Hb 65 per cent (9·6 g. per cent). R.B.C. 4,430,000 per c.mm. Colour index 0·74. P.C.V. 37 per cent. M.C.V. 84 c.u. M.C.H.C. 25·59 per cent. W.B.C. 9,600 per c.mm. *Differential Count*: P. Neutrophils 60 per cent. Lymphocytes 34 per cent. Monocytes 3 per cent. P. Eosinophils 3 per cent. *Plasma-proteins*: Fibrinogen 0·92 g. per cent. Globulin 1·5 g. per cent. Albumen 3·8 g. per cent. Total 6·22 g. per cent.

Fæces.—Gregerson's slide test for occult blood: Positive. Microscopical examination of fæces: Numerous partially digested muscle-fibres seen. Total fat 10·8 per cent of dried fæces. Of the total fat, 95·37 per cent was split, 4·63 per cent unsplit.

The second laparotomy was carried out on Feb. 8. The upper jejunum was dilated. The bowel of the excluded loop, including the anastomosis, was thickened and hard and it seemed that there had been considerable progression of the condition since the original laparotomy in September, 1951. Large hard glandular masses were noted in the mesentery and numerous omental and parietal adhesions held the loop in the left flank. The adhesions were divided and ligated and the excluded loop, together with the original anastomosis and a segment of mesentery to include the glands, was resected. An end-to-end anastomosis was performed using two layers of continuous catgut. One pint of blood was transfused

during the operation. Post-operatively he was given a short course of penicillin, and nasogastric suction and intravenous therapy were maintained for twenty-four hours, after which he was allowed to drink. Convalescence was once again uneventful. He was discharged on Feb. 25.

The pathologist's report showed that, in all, 3 ft. of jejunum had been removed. Two strictures were found at the site of adherent omentum. Incision of the strictures showed local thickening and ulceration of the bowel wall. The mesenteric glandular masses were succulent and some showed necrosis in the centre. The histological appearances were those of reticulum-cell sarcoma with gross superadded infection (*Fig.* 178).

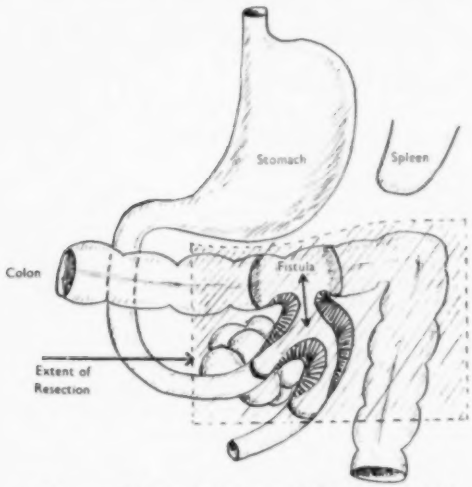

FIG. 179.—Diagram showing state of affairs found at third laparotomy (April, 1953). Recurrence of reticulosarcoma with jejuno-colic fistula and glandular enlargement. Shaded area shows extent of resection.

He was again kept under observation at the Out-patient Department. For some months he felt well and put on weight and was fit for light work. By April, 1953, he was again complaining of abdominal pain, anorexia, and loss of weight. On examination there was a palpable tender thickening beneath the scar. Barium examination suggested a 7-in. long recurrence in the upper jejunum.

After a good deal of heart-searching on the part of both patient and surgeon it was decided to undertake a further laparotomy to see whether more radical surgery was feasible. Radiography of the chest showed no evidence of metastases or other pulmonary lesion.

A third laparotomy was performed on April 28, 1953. The old scar was excised and on entering the abdomen the sarcoma was found to have recurred 4 in. from the duodenojejunal flexure. The affected loop was tucked up beneath the left half of the transverse colon where a jejunocolic fistula had formed (*Fig.* 179). Numerous enlarged glands were seen in the mesentery. Segments of colon and jejunum were excised, as shown, together with a mass of adherent omentum. The mesenteric glands were also removed in the jejunocolic segment. The anatomy was then reconstituted (*Fig.* 180) by end-to-end anastomosis of the colon (interrupted silk sutures) and jejunum (continuous catgut), with closure of the mesenteric gap. One pint of dextran was transfused during the operation. Post-operative treatment was on similar lines as on previous occasions.

On the fifth post-operative day he began to complain of pain over the left lower ribs, aggravated by deep breathing. Auscultation showed no evidence of consolidation. Two days later there was a left basal friction rub and the temperature rose sharply to 103° F. The white-cell count was 18,700 per c.mm. Chest radiographs showed inflammatory change in the left lower zone, with a small basal pleural effusion. Air was defined under the diaphragm and several fluid levels were noted but they were presumably related to stomach and colon.

On the following day (May 6) a small gridiron incision was made in the left hypochondrium, and on opening the posterior sheath a large quantity of foul gas escaped from an abscess cavity. No fluid pus was present, but the lining consisted of yellow slough. The cavity corresponded to a dilated left anterior subphrenic space. The small incision was sutured around a Penrose drain.

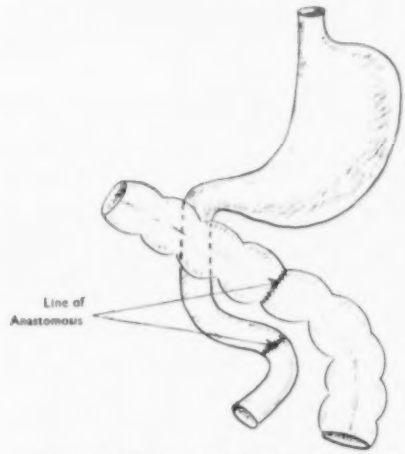

FIG. 180.—Diagram showing final state after resection and reconstitution.

Subsequent progress was uncomplicated and he was discharged from hospital on June 1.

The pathologist's report confirmed recurrence of the reticulosarcoma.

Since this time the patient has remained fit and well and has returned to full employment. When last seen at the Out-patient Department early in 1950, he had no complaints and there was no evidence of recurrence.

No radiotherapy was given at any time.

COMMENT

This is a case of reticulosarcoma of small bowel in which the symptomatology suggested peptic ulcer of the stomach. Radiology did not help to elucidate the diagnosis and the lesion was first brought to light by the advent of perforation and peritonitis. Even at laparotomy it was not possible to make the diagnosis on clinical grounds. The lesson to be drawn from this is that sarcoma of the small intestine should be suspected at laparotomy even if thickening of the bowel extends over a considerable length and there is no localized palpable mass and also where a perforation of the bowel appears to have occurred in an area of acute enteritis.

The second interesting feature of the case is that the patient is still fit and well more than seven and a half years after the onset of symptoms. The prognosis in sarcoma "though usually unpredictable, is not always unfavourable" (Henderson and Main, 1954).

Thirdly, it would have been to some extent justifiable to regard the situation at the third laparotomy as representing a progressive malignant tumour which was inoperable because of its early recurrence, its penetration of a neighbouring viscus, its proximity to the duodenum, and the awkward situation of the glandular masses near the main mesenteric vessels.

A tenacious and radical attitude in this case would appear to have been justified by the subsequent outcome.

I am grateful to Dr. R. Rankin, Area Consultant Pathologist, for the pathological reports and microphotograph.

REFERENCES

AIRD, I. (1949), *A Companion in Surgical Studies*, p. 701. Edinburgh: E. & S. Livingstone Ltd.
HENDERSON, R. G., and MAIN, R. G. (1954), *Brit. J. Surg.*, **42**, 268.
IRVINE, W. T., and JOHNSTONE, J. M. (1955), *Ibid.*, **42**, 611.

THE PREPYLORIC SEPTUM: A RARE ANOMALY

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THE stomach enjoys a peculiar freedom from the majority of malformations which affect the digestive tract, but among the rarer anomalies must be placed the presence of a mucosal diaphragm of the pyloric antrum. Since 1949, 5 cases have been reported in adults, and 2 further cases are described below. The morbid anatomy, clinical features, and X-ray appearances are so remarkably constant that the condition merits recognition as a specific entity.

FIG. 181.—Diagram of the prepyloric septum.

A thin diaphragm, consisting wholly of mucosa, and containing neither muscle nor fibrous tissue, is found approximately 2 cm. proximal to the pylorus. A small orifice, 2–3 mm. in diameter, is present in the diaphragm, usually situated to one side of its centre, the edge being soft and free from fibrosis, but of sufficient strength to resist dilatation (*Fig.* 181).

HISTORY

Although the condition is almost certainly congenital in origin, it has only twice been reported in infants. The first case was described by Bonner in 1912, but there is some doubt as to whether in fact a true prepyloric diaphragm was present. The child was 4 weeks old and presented with pyloric obstruction, for which a gastro-enterostomy was performed. It was noted that the pyloric sphincter was hypertrophied at operation. The child died on the sixteenth day and at post mortem it was found to have hypertrophic pyloric stenosis, but, in addition, a fold of mucosa was found to occlude the antrum, forming a valvular obstruction which in some ways corresponded to a prepyloric diaphragm.

The second case was that of an imperforate prepyloric diaphragm occurring in a newborn infant and described by Touroff and Sussman in 1940. At operation on the fifth day after birth the pyloric antrum was found to be occluded by an imperforate mucosal diaphragm approximately 1½ cm. proximal to the sphincter. The diaphragm contained no muscle and was formed of normal gastric mucosa. It was incised radially and a pyloroplasty performed. After a stormy post-operative course the child survived and was well and free from symptoms seventeen months later.

The first case to be recorded in an adult was described by Sames in 1949. A woman aged 40 years, with a six-years' history of dyspepsia, was found to have a gastric ulcer. A barium meal confirmed the presence of an ulcer on the lesser curvature and also demonstrated a prepyloric diaphragm which appeared as a thin knife-like filling defect. There was no obstruction either clinically or to the passage of barium. A subtotal gastrectomy was performed. On examining the stomach the diaphragm was found to be 3 mm. in thickness, consisting of mucosa and submucosa only, situated 1½ cm. proximal to the pylorus. The stoma was 3 mm. in diameter and was situated eccentrically, slightly towards the greater curvature.

In 1953 a case of prepyloric diaphragm by obstructive episodes was reported by Rota from Ottawa. The patient was a woman, aged 74 years, complaining of intermittent vomiting over the preceding eight years. Partial gastrectomy was performed, from which the patient made an uneventful recovery and was free from symptoms thirteen months later. The diaphragm was immediately proximal to the pylorus, the central opening being 4 mm. in diameter. Chronic antral gastritis was present.

Later in 1953 a further case was reported by Gross and Durham. As in the preceding case, the patient complained of intermittent vomiting of obstructive type, without pain. The diaphragm was clearly

demonstrated pre-operatively by a barium meal. At operation the diaphragm was found to be 2 cm. from the pylorus, the central opening being 3–4 mm. in diameter. The membrane was incised and a Finney pyloroplasty performed.

The first case to be recognized by X-ray examination and operated upon (in 1946) was published by Albot and Magnier in 1955. The three preceding papers were reviewed and a further case of "le diaphragme muqueux antro-pylorique" added. This occurred in a man, aged 32 years, suffering from periodic epigastric pain and vomiting over the preceding three years. Barium-meal examination demonstrated the diaphragm quite clearly as "un étranglement linéaire de l'antre".

The appearances were commented upon in a separate paper (Albot, Renaux, and Girard, 1946). At operation the same year the diaphragm was demonstrated, but neither the operative detail nor the morbid anatomy is fully described.

A further case was described by Swartz and Shepard in 1956, in a woman aged 55 years, giving an eight months' history of loss of weight and progressive vomiting. The diaphragm was again easily demonstrated, and at operation it was found to be 7 cm. proximal to the pylorus, with a central perforation 1 cm. in diameter. A pyloroplasty was performed and her condition six months later was satisfactory.

INCIDENCE

Clearly the condition is very rare, but it seems likely that in the past many cases have passed unrecognized or have been considered as unusual forms of pyloric stenosis.

In a series of 2625 post-mortem examinations in adults at the Royal Hospital, Sheffield, extending over the last ten years, the condition has not been demonstrated in any autopsy. In this series the stomach was examined in all cases.

MORBID ANATOMY

The abnormality is essentially one of the mucosa and submucosa only. The muscular wall of the stomach, apart from the muscularis mucosæ, takes no part in the diaphragm, which consists of apparently normal mucosa on both surfaces, the space between being filled with loose connective tissue (*Fig.* 183).

The position of the diaphragm is remarkably constant, being nearly always about 2 cm. proximal to the pylorus. In the nature of things this measurement can only be approximate when seen at laparotomy, and in the resected specimen the elasticity of the stomach allows a good deal of latitude in its determination. However, the septum has never been reported proximal to the antrum and there is always an easily recognizable and distinct portion of the antrum between the septum and the pylorus.

Sometimes the position of the septum is marked by an ill-defined groove on the serous surface of the stomach (Sames, 1949).

The orifice in the septum may be central or slightly eccentric, usually somewhat towards the lesser curvature. It is usually surprisingly small, about 2–3 mm. Although the edges are soft and free from fibrosis the opening resists dilatation, but the septum can be ruptured forcibly with the finger. Superficial erosion of the mucosa at the orifice has been described, but this seems to be a secondary condition associated with trauma from attempted passage of food or trauma from the pyloric sphincter. No submucous fibrosis is found around the orifice.

Obstruction tends to occur in episodes, possibly associated with gastritis; and hypertrophy of the body of the stomach, corresponding to that found in pyloric stenosis, is not a feature of the condition.

The septum is to some extent mobile, pressure from the proximal aspect causing it to bulge down to and against the pylorus and pressure from the pyloric side causing it to balloon into the body of the stomach.

ORIGIN

There can be no doubt that this is, in fact, a congenital anomaly.

Septa and atresias occur in other parts of the alimentary canal, more commonly in the œsophagus, duodenum, right colon, and anus. It might be supposed that a prepyloric septum would present at birth or in childhood, but if the central orifice is large enough to allow food to pass, there is no reason why symptoms should become apparent. In practice it is found that these cases present in middle age, and it is reasonable to suppose that obstruction is precipitated by gastritis leading to œdema of the orifice in the septum, with consequent narrowing.

Such stenosis may aggravate the gastritis, thus prolonging the episode of obstruction. Septa in the colon and elsewhere may also present for the first time in adult life (Reid, 1948).

In the embryo the mucosa of the foregut is derived from endoderm, while the muscular coat is derived from mesenchyme. Towards the end of the second month the epithelial lining of the gut grows far more rapidly than the muscle layers, and the lumen appears to be obliterated by masses of epithelial cells. After this, as the muscular layers also enlarge, vacuoles appear in the centre of the gut, which coalesce to form the definitive lumen. The stomach becomes a recognizable structure about the sixth week, and the apparent occlusion of the lumen of the foregut is most marked in the narrower œsophagus and upper small intestine (Patten, 1946; Arey, 1954). It is suggested that the persistence of the epithelial occlusion may become the prepyloric diaphragm. In support of this hypothesis it is observed that the narrower portions of the foregut, the duodenum and œsophagus, are the more common sites for the presence of septa and that the pyloric antrum, being the narrowest part of the stomach, might be expected to be the site of septa produced in the same manner. (No case could be found in the literature of septa or atresia of the body of the stomach.)

In considering the possibility of the septum being acquired, the absence of fibrosis and the lack of any direct relationship to gastric ulceration is apparent. The septum is entirely dissimilar to the condition of hour-glass stomach, nor can it be related to persistence of muscle spasm as the muscular wall takes no part in its structure. There is, however, a further possibility which merits consideration. Prolapse of the gastric mucosa through the pylorus is known to occur and can be demonstrated by barium-meal examination (Kaplan and Shepard, 1951). It may produce a variety of symptoms which cannot be differentiated

clinically from those caused by other gastric lesions. It is conceivable that such mucosal folds, when exiled from their normal gastric environment, might become inflamed and, eventually, by contraction of scar tissue return to the pyloric antrum as a septum (Rota, 1953). However, when the softness and freedom from fibrosis and ulceration of the septum is considered, together with the fact that it has never been reported in a known case of mucosal prolapse, this theory of its origin becomes untenable.

It is known that the condition can be congenital in origin, from the case described by Touroff and Sussman (1940), and the weight of evidence at the present time suggests that all cases are congenital.

CLINICAL FEATURES

The condition usually presents in middle age. The average age in the recorded cases is 51. In this small series women were more commonly affected than men—in the ratio of 4 : 3.

The most constant feature is vomiting, which was present in every case. The vomiting, which is intermittent—often with long periods of complete remission—usually occurs immediately after taking food and consists of the food which has just been eaten. The copious, effortless vomiting of pyloric stenosis is not a feature of the condition. Nausea usually precedes the vomiting. Bile is absent from the vomitus.

Pain is a variable feature. In some cases it is entirely absent; in others there may be a feeling of epigastric fullness, amounting to discomfort, immediately after food, or true post-cibal epigastric pain may be present.

Anorexia and weight loss are common and this, together with the vomiting, usually brings the patient to investigation under the suspicion of a pyloric carcinoma.

No case of hæmatemesis or melæna has been recorded in association with the condition, except in Sames's case (1949), which was complicated by the presence of a gastric ulcer.

Physical examination is essentially negative. No abnormal physical signs have been described.

In general the clinical picture is one of gastritis associated with somewhat atypical intermittent vomiting and weight loss.

X-ray Appearances.—These are remarkably constant and have been observed in all the recorded cases, although this has not always led to preoperative recognition of the condition.

Barium outlines the body of the stomach, which is usually of normal size, and passes through the diaphragm into the pyloric antrum without difficulty. In spite of clinical evidence of obstruction at the orifice in the septum, there seems little difficulty in filling the antrum beyond it with barium. This may, perhaps, be due to preparation of the stomach for the examination. The septum is then outlined as a thin, constant, knife-like filling defect, occurring 1–2 cm. proximal to the sphincter. The appearances are characteristic, both on account of the constancy of the position and the thinness of the defect, which is truly linear. The defect is demonstrable in all projections regardless of the position of the patient. The duodenal cap and the sphincter itself are normal in appearance (*Fig.* 182).

The findings have to be differentiated from redundancy of the gastric mucosa, with or without prolapse through the pylorus, cicatricial scarring from old gastric ulceration, ectopic smooth muscle in the gastric mucosa, and spasm.

Gastroscopy.—This has not been reported on previously. In one of the cases here described the appearances were normal. In view of the difficulty in visualizing the antrum, and of the presence of normal mucosa forming the septum, normal appearances are to be expected.

TREATMENT

From a theoretical standpoint gastrotomy and simple excision of the septum should be the treatment of choice. The absence of ulceration, hyperacidity, and pyloric stenosis renders gastrectomy or any form of pyloroplasty unnecessary.

In practice the condition is met with so rarely that it is seldom recognized until the stomach, and possibly the duodenum also, has been opened. Where the septum has been excised, or incised radially, the results have been satisfactory. In those cases reported from across the Atlantic a pyloroplasty has been added, but this seems to have been done as a result of a somewhat illogical association between pyloroplasty and pyloric obstruction generally.

At laparotomy the condition can seldom be diagnosed from the external appearances of the stomach. However, from the patient's clinical features and X-ray appearances it is usually clear that a pyloric lesion is present, and in such circumstances the logical procedure is to perform a Billroth I type of gastrectomy, leaving the exact pathology to be determined from the specimen. At the present time neither the mortality nor the morbidity from such a course should be any higher than that of any other operative procedure and a great deal of time and difficulty can be saved thereby.

CASE REPORTS

Case 1.—This patient was admitted to Manchester Royal Infirmary under the care of Mr. R. L. Holt with a history of twelve years' abdominal discomfort. He was suspected of having a duodenal ulcer in 1944 and was treated for duodenal dyspepsia by his own doctor. It was not until 1956 that he had several acute attacks of pain. He was referred at that time to the Manchester Royal Infirmary and a barium-meal report was: "The stomach appeared to be normal. The duodenum was tender and slightly deformed although no ulcer crater was seen. The appearances were suggestive of duodenal ulceration."

He continued to have upper abdominal discomfort which became almost continuous. He stated that the pain was made worse by cold, work, or anxiety and was relieved by warmth, rest, milk, and antacids. Although he occasionally had a little nausea, he was very rarely sick. On abdominal examination there was no abnormality to be made out.

At Operation.—He was operated upon on Jan. 8, 1958. The duodenum appeared completely normal and there was no evidence externally of any pathology. In view of the persistence of his symptoms the pyloric segment of the stomach was opened. A most unusual condition was found in which, although the mucosa looked completely normal, the opening between the pylorus and duodenum was only a few millimetres wide. There was no evidence of any hypertrophy of the pyloric sphincter nor of the gastric musculature. It was thought that the stenosis was due to a congenital narrowing of the

mucous lining of the pylorus. The membrane was excised and the duodenum inspected without finding any evidence of previous ulceration.

His convalescence was uneventful and he was seen in the follow-up clinic on April 22, 1958, when he appeared to be practically symptom-free.

Case 2.—The patient, a man aged 68 years, was admitted to the Royal Hospital, Sheffield, under the care of Mr. H. Blacow Yates, with a history of sporadic

FIG. 182.—X-ray appearance of the septum in *Case* 2.

FIG. 183.—Appearance of the septum in *Case* 2 from the operation specimen.

episodes of epigastric pain and vomiting over the last eighteen years. The pain and vomiting were induced by food, especially meat. His pain was relieved as soon as he had vomited. Each episode lasted two to three days and in the preceding three months they had become more severe. His appetite was good. Physical examination revealed nothing abnormal.

Gastroscopy was performed, giving a good view of the stomach with full penetration towards the antrum. No abnormality of the gastric mucosa was seen and peristalsis appeared to be active and, although slightly asymmetrical, to involve the whole circumference of the stomach. No significant abnormality was revealed.

Barium-meal examination showed an indefinite filling defect in the pyloric antrum. This was repeated three months later, and on these films the septum was clearly visualized (*Fig.* 182). The examination was reported on as follows: "A band-like deformity is still present in the pyloric antrum. The peristaltic waves up to, and beyond, this point were quite normal. A barium residue was still present in the 24 hour film. *Conclusion*: The delayed passage of barium suggests that the deformity in the pyloric antrum is, in fact, a stricture, probably the result of an old healed gastric ulcer."

AT OPERATION.—Laparotomy was undertaken through a median incision on April 22, 1958. The gall-bladder was found to be full of stones and was removed. The pyloric antrum was somewhat thickened to palpation, although quite soft and mobile. The stomach was of normal size and not hypertrophied. It was clear that the antrum was abnormal and, in view of the history and radiological findings, a low Billroth I partial gastrectomy was performed. Recovery was uneventful.

Examination of the specimen showed that the thickening previously felt consisted of a thin mucosal septum 2·5 cm. from the pylorus, containing a central orifice 3 mm. in diameter, which was quite soft and free from ulceration or fibrosis. A finger could be passed through the pylorus and the septum palpated with the finger-tip. The orifice resisted gentle dilatation with forceps. On filling the stomach with water it barely passed through the septum, passing out as a slow drip. There was no gastritis and the distal part of the antrum beyond the septum was normal in appearance (*Figs.* 183, 184).

DISCUSSION

The first case here recorded is not entirely typical of the condition in so far as the septum was unusually near the pylorus. Simple excision of the membrane was sufficient to effect a cure. The X-ray appearances were not sufficiently definite to warrant a pre-operative diagnosis, possibly because of the proximity of the septum to the sphincter.

In the second case the clinical features were complicated by the presence of gall-stones, and in

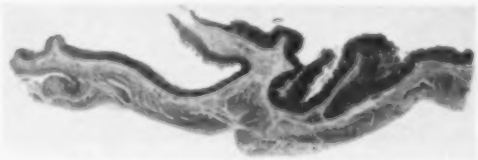

FIG. 184.—Photomicrograph of the septum in *Case* 2.

this respect it is comparable to Sames's original case, which was associated with a gastric ulcer. There is little doubt that most of his symptoms were attributable to the septum. It is likely that during his periods of freedom from symptoms the gastric mucosa was healthy, and that the opening in the septum was adequate to transmit the gastric contents. During his exacerbations it may be supposed that gastritis involved the mucosa of the septum, causing œdema and further occlusion of the opening, with consequent gastric stasis and vomiting. The history and clinical and X-ray findings were typical of the condition.

Although the condition is one of extreme simplicity, both in its morbid anatomy and cure, the prognosis in the untreated case is probably very bad, being comparable to that of severe pyloric stenosis.

SUMMARY

1. The history and recorded cases of prepyloric mucosal diaphragm are reviewed.

2. The morbid anatomy is described.

3. The probable origin of the condition is discussed.

4. The clinical features and X-ray appearances are described.

5. Two further cases are recorded.

Acknowledgements.—It is a great pleasure to acknowledge the help of Mr. H. Blacow Yates in preparing this paper and in allowing me to publish *Case* 2. I am also indebted to Mr. R. L. Holt for his kindness in allowing me to record *Case* 1, which was treated under his care in the Manchester Royal Infirmary. My thanks are also due to Dr. J. L. Edwards for the pathological examination of the stomach in *Case* 2 and for his figures on the incidence of the condition and for his assistance, and that of Mr. W. J. Lytle, in preparing this paper. I would also like to thank Dr. T. Lodge for the X-ray plates and report in *Case* 2, and Miss D. E. Rowling for the illustrations.

REFERENCES

ALBOT, G., and MAGNIER, F. (1955), *Arch. Mal. App. dig.*, **44**, 1162.
— — RENAUX, J., and GIRARD, E. (1946), *Ibid.*, **35**, 118.
AREY, L. B. (1954), *Developmental Anatomy*. London: W. B. Saunders Co.
BONNER, A. (1912), *N. Y. Post-grad.*, **27**, 1118.
GROSS, K. E., and DURHAM, M. W. (1953), *Radiology*, **61**, 368.
KAPLAN, I. W., and SHEPARD, R. M. (1951), *J. Amer. med. Ass.*, **147**, 554.
PATTEN, B. M. (1946), *Human Embryology*. London: J. & A. Churchill.
REID, D. R. K. (1948), *Brit. J. Surg.*, **36**, 52.
ROTA, A. N. (1953), *Arch. Path. (Lab. Med.)*, **55**, 223.
SAMES, C. P. (1949), *Brit. J. Surg.*, **37**, 244.
SWARTZ, W. T., and SHEPARD, R. D. (1956), *J. Ky St. med. Ass.*, **54**, 149.
TOUROFF, A. S. W., and SUSSMAN, R. M. (1940), *Surgery*, **8**, 739.

PSEUDOMYXOMA PERITONEI ASSOCIATED WITH AN APPENDIX OBSTRUCTED BY AN ARGENTAFFINOMA (CARCINOID) IN A MALE

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MUCOCELE of the appendix, a curious, ill-understood and uncommon condition, is of particular interest because of the peculiar and serious complication this lesion infrequently occasions. Although it is generally agreed that pseudomyxoma peritonei of appendiceal origin is rare, Collins (1955), as a result of studying 50,000 appendices, mostly obtained from appendicectomy cases, assessed its occurrence as 0·54 per cent of these specimens. Such an incidence is more than twice that generally expressed for mucocele of the appendix.

Castle (1915) collected the post-mortem reports of various authors and concluded that the incidence of mucocele of the appendix was 0·2 per cent of 13,158 necropsies. Weaver (1937), studying appendicectomy specimens, discovered mucocele in 0·11 per cent of a series of 6225 cases. According to Woodruff and McDonald (1940), only in 0·3 per cent of 43,000 cases of appendicectomy at the Mayo Clinic was there evidence of mucocele; and in none of these instances did pseudomyxoma peritonei develop. Among 3087 appendices removed at operation, Timoney (1944) discovered only 4 cases of mucocele, 1 of which was complicated by the development of pseudomyxoma peritonei.

At the David Lewis Northern Hospital, Liverpool, the examination of an unselected, consecutive series of 1146 appendices removed at operation disclosed mucocele in 0·28 per cent of specimens; the incidence of carcinoid tumour in the series was nearly twice as much, viz., 0·6 per cent. In 2 cases, including the one to be presented below, such a tumour had caused a cystic condition to develop in the distal portion of the appendix.

The type of obstructing, causal agent usually described in mucocele of the appendix is either inspissated mucus, foreign body, periappendiceal adhesions with kinking, intussusception (McCormick, 1957), fæcolith (Carleton, 1955), normal involution (Phemister, 1915), or, much more commonly, contracting fibrous tissue due to previous inflammation (Woodruff and McDonald, 1940; Carleton, 1955). Certainly a carcinoid tumour is capable of blocking the appendiceal lumen, but such a growth has been described only occasionally as the initiating cause of mucocele (Topping, 1928; Carleton, 1955; Elliot, 1957). Rare lesions responsible for the production of appendiceal mucocele include early carcinoma of the cæcum (Muir, 1931), infiltrating adenocarcinoma at the base of the appendix (Lesnick and Miller, 1949), and endometrioma of the cæcum causing, by means of a scleral reaction, blockage of the lumen (Shemilt, 1949).

In the female, ovarian pseudomucinous cystadenoma is the commonest source of pseudomyxoma peritonei. This type of gonadal lesion is sometimes accompanied by a mucocele of the appendix, and because of such an association many authorities have presumed the endodermal essentialness of ovarian pseudomucinous epithelium. In the absence of pseudomyxoma peritonei the concurrence, particularly of a pseudomucinous cystadenoma of the ovary and mucocele of the appendix, is probably due to the coexistence of two independent lesions. Following

rupture of an ovarian pseudomucinous cystadenoma the ensuing pseudomyxoma peritonei may involve the appendix, causing obstruction of its lumen and subsequently the formation of a mucocele.

In the case of pseudomyxoma peritonei of appendiceal origin, about to be described, not only is it believed that the mucocele was initiated by an argentaffinoma but, in addition, it is considered that this carcinoid tumour, by infiltrating, and thereby weakening, the distended appendiceal wall, played an important part in provoking the rupture which led to the progressive, diffuse type of incapacitating, mucinous intraperitoneal complication.

Although the mechanism whereby pseudomyxoma peritonei of appendiceal origin is initiated and maintained remains debatable, histological evidence in this case supports the thesis which postulates that it is the spill of viable mucous cells from the mucosa of the appendix into the cœlomic cavity, the consequent attachment of the cells to the mesothelial lining, and their continued proliferation and secretory activity which are responsible for this intraperitoneal condition.

Of interest, too, like several other instances of this condition (Wilson, 1912; Unger and Paradny, 1956; and others), is the mode of its presentation and the establishment of the diagnosis during inguinal herniorrhaphy.

CASE REPORT

Clinical Features.—The patient, a male 40 years of age, complained of local pain and inconvenience due to a right inguinal hernia. A herniorrhaphy was undertaken in September, 1955. At this operation the sac was exposed, in routine fashion, and on opening it a considerable quantity of mucinous ascitic fluid escaped. Digital examination of the right iliac fossa through the neck of the sac revealed a tumefaction. The inguinal canal was repaired and the operation was completed.

Subsequently when a formal laparotomy was performed it was found that the whole of the peritoneal cavity was filled with a mucinous fluid adherent to every organ; there was a particularly large accumulation in the region of the cœliac axis, and as much of this as possible was delivered manually. The omentum appeared to be extensively infiltrated by a mucinous growth. A large tumefaction involved the appendix; this, together with the appendix, was removed with some difficulty, since it was partly fixed to the bladder and rectum. At operation the liver was essentially normal.

Examination of the specimen removed at operation showed that it was a thickened appendix stump obstructed near its base by a solid yellowish tumour which had infiltrated through all the coats of this viscus. Beyond the point of obstruction the appendix had been distended into a mucocele measuring 15 × 5 cm. and which, having ruptured some time before operation, had its mucosal aspect, in its entirety, exposed to the peritoneal cavity. The whole of the peritoneal surface of the ragged and torn mucocele was covered by adhesions, which had attached it to the pelvic wall and organs, and pseudomucinous deposits. Apart from some trabeculation the inside of the broken sac was smooth.

Commencing during the otherwise uneventful postoperative course and continuing into the convalescent period, the patient was repeatedly examined and the following investigations were carried out:—

1. Except for a number of diverticula situated in the pelvic colon, a barium enema and a follow-through barium meal showed no evidence of a gastro-intestinal lesion.

2. Clinical and radiological examination of the chest, although revealing an elevated hemidiaphragm on the right side, failed to confirm any intrinsic thoracic lesion.

3. The blood-picture was found to be essentially normal.

4. Employing a chromatographic method an amount of 5 H.I.A.A. in excess of normal was demonstrated in the urine.

The patient admitted later, at a follow-up clinic, that some months prior to his operation he had suffered from occasional bouts of diarrhœa. These attacks continued sporadically and were attributed by the patient to the dysentery he contracted in Egypt 12 years previously. Microscopical and bacteriological examination of his stools and blood revealed no obvious cause for these attacks. Moreover the diarrhœa was not associated with episodic cyanosis or bronchial asthma; and there was no evidence of pulmonary stenosis or any other feature of the carcinoid syndrome. He continued, however, to excrete in his urine amounts of 5 H.I.A.A. in excess of normal.

Three months after operation ascites could be demonstrated clinically and within 6 months he was re-admitted to hospital for paracentesis; this procedure was repeated at monthly intervals. On each occasion 15–20 pints of mucinous fluid was removed from his peritoneal cavity. Apart from mucin and cells of mesothelial derivation the ascitic fluid contained also epithelial elements of intestinal aspect (*Figs.* 187, 188). The patient's diarrhœa abated completely, but gradually his peritoneal cavity became grossly distended with fluid, and multiple hard masses could be felt in every part of his abdomen. Owing to loculation and the development of palpable intraperitoneal masses paracentesis became progressively more difficult to perform until aspiration was possible only after the introduction of streptokinase into the cœlomic cavity. His response to abdominal X-radiation was disappointing, though it relieved the coexistent œdema of the legs. Now, three years after the initial operation, his tense, solid abdomen is grossly distended, dull to percussion in all areas, and is so large that it dwarfs the remainder of his body. His markedly distended belly is supported by a corset. Despite his increasing debility and inability to walk more than a few yards without stopping for a rest, he remains mentally alert and anxious to continue his work as a shop assistant.

Morphological Features.—The tumour obstructing the base of the appendix was an argentaffinoma of typical histological appearance (Winston Evans, 1956); it was well demarcated and extended deeply into the muscle coats to reach the subserosa (*Figs.* 185, 186). A marked argentaffin reaction (Masson) was exhibited by the majority of the neoplastic cells, which reacted positively also when the Gibbs and diazo techniques were employed.

The appendiceal lumen was completely blocked, stoppered like a bottle, for the carcinoid protruded into it as a circumscribed, bulbous swelling (nearly a centimetre in diameter) attached by a wide, stumpy, traction stalk composed of invaded smooth muscle. The surface of the new growth was covered by grossly infiltrated, attenuated, and partly ulcerated mucosa.

The wall of the ruptured mucocele was devoid of an epithelial lining almost throughout its entire extent. Only in the acute angle formed between the bulbous, protuberant argentaffinomatous tumour (*Fig.* 185) and the interior surface of the appendix could any epithelial covering be demonstrated; in this zone a pseudostratified layer of columnar, sometimes hypertrophied mucus-secreting cells extended partly over the carcinoid areas and distally over the internal wall of the appendix for a distance of scarcely 0·5 cm. Elsewhere the mucocele wall consisted of a congested, thickened, vascular serosa and subserosa occasionally studded with collections of lymphocytes, a muscularis propria mostly but patchily

replaced by hyalinized, occasionally œdematous, tissue containing widely scattered tiny foci of calcification and an inner lining of hyaline fibrous tissue in which, here and there, occurred deposits of calcium and remnants of degenerate epithelial cells. Scattered at considerable intervals in the wall of the mucocele were microcysts walled by compressed stromal tissue and distended by mucin. Within these cystic spaces no cells or cellular debris could be distinguished.

Attached to the outer wall of the mucocele were polypoid masses of pseudomucinous tissue consisting of a

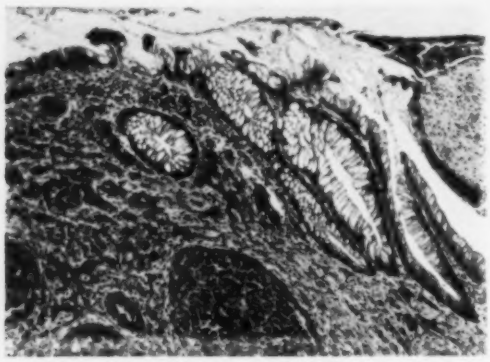

FIG. 185.—Appendiceal carcinoid tumour bounded by actively mucus-secreting cells, some of which are disposed in early papillary formations. H. and E. (×72).

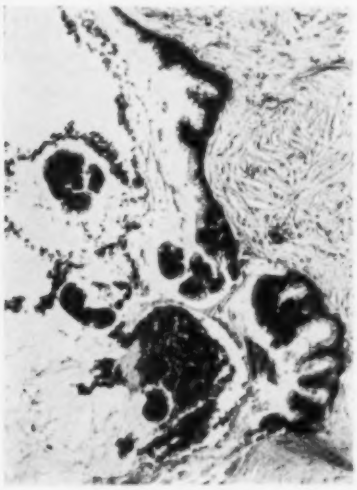

FIG. 187.—Glandular mucus-secreting epithelium resembling that of the appendix lining the wall of a pseudomyxomatous mass attached to outer wall of mucocele. H. and E. ×87.)

fibrous stalk, occasionally infiltrated by lymphocytes from which delicate arborescent septa extended to enclose small and large pools of homogeneous amorphous mucin. Here and there, usually adherent to the trabeculæ, were found mucinous, uniformly tall columnar and goblet cells disposed in a single row tending to line large cystic spaces. Sometimes these epithelial cells occurred in small papillary and acinar formations suggesting a glandular origin (*Figs.* 187, 188); at other times they appeared scattered in small aggregations lying loosely amid pools of mucin; occasionally they were reminiscent of those ordinarily seen in ovarian pseudomucinous cystadenomata (*Figs.* 188, 189).

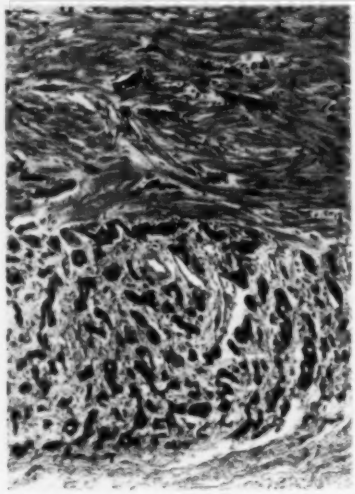

FIG. 186.—Clumps of carcinoid tissue infiltrating muscle and spreading in the serosa. H. and E. (× 82.)

FIG. 188.—Mucin-secreting epithelium lining gelatinous deposit in mesentery. H. and E. (× 120.)

Similar masses, adherent to the mesentery, presented identical microscopical features. In these, as in the mucinous polypi attached to the serosal surface of the mucocele, the epithelium exhibited only sparse, argentaffin cells (*Fig.* 190) occurring at widely separated intervals. In none of the gelatinous masses examined were there any macroscopical or microscopical foci of calcification.

The hernial sac was composed of a laminated fibrovascular wall and fatty tissue showing foci of lymphocytic

infiltration. No gelatinous deposits were found adherent to the lining of the sac.

DISCUSSION

Although the pathogenesis of mucocele of the appendix and of its complication, pseudomyxoma peritonei, is largely still a matter of conjecture, it is generally believed that, following the proximal, progressive narrowing or blocking of the appendiceal lumen, the glands distal to the site of partial or complete occlusion are presumed to secrete enough mucus to expand gradually this viscus. Subsequently the accumulated gelatinous material, because of the pressure it and the increased muscular activity (Wilson, 1950) exert, so attenuates the mucosa that the epithelial elements are largely, if not entirely, destroyed. Eventually, probably after many months, most of the muscularis is replaced by hyalinized fibrous tissue and the appendix distended into a thin-walled cyst. Hernial protrusions, through the stretched and poorly nourished wall of the appendiceal mucocele, develop into diverticula; and it is the rupture of these structures that is considered to be the precipitating cause of the ensuing pseudomyxoma peritonei.

There is some experimental evidence for such a train of events, since the studies of Wells (1937), Grodinsky and Rubnitz (1941), Rubnitz and Hermann (1943), and Cheng (1949) have shown that when the appendix of a rabbit is ligated near its base in such a way as to produce little interference with its blood-supply, appendiceal mucoceles of various sizes can be induced. When such an experimentally produced mucocele is allowed to remain long enough in the

FIG. 189.—High-power view of *Fig.* 188 showing pseudo-mucinous-like epithelium. H. and E. (×240.)

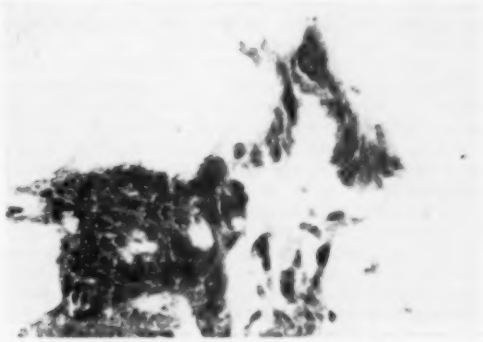

FIG. 190.—Scanty argentaffin cells in deposits found in ascitic fluid. Masson's silver. (×240.)

FIG. 191.—Early mucocele of appendix, showing transition to actively mucin-secreting surface epithelium and intramural glands. H. and E. (×75.)

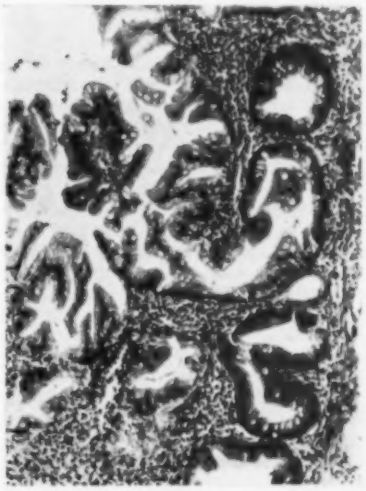

FIG. 192.—Papillary transformation of appendiceal epithelium in an early mucocele. H. and E. (×75.)

peritoneal cavity or is ruptured artificially, a condition of pseudomyxoma peritonei often develops.

In man the spilling of the mucinous contents of a cystic appendix into the peritoneal cavity, though a distinctly uncommon event, can result from a neoplasm infiltrating, and thereby weakening, the mucocele wall. Doubtless, in the case described above the blocking agent which initiated the production of the mucocele was the appendiceal carcinoid tumour. Intramural invasion of the cystic viscus, especially in the zone immediately surrounding the site of origin of the tumour, by clumps, columns, and strands of argentaffinomatous tissue (*Figs.* 185, 186), was a factor important in facilitating rupture. Extrusion of the mucinous contents then led to an intractable, diffuse progressive pseudomyxoma peritonei.

Many writers, including D'Aunoy and Fine (1934), are of the opinion that pseudomyxoma peritonei of appendiceal origin results from an 'adenocystoma' of this organ. Whether pseudomyxoma peritonei of such a derivation is in itself a truly neoplastic process is still debatable. Certainly the paucity of cells usually noticed in the intraperitoneal gelatinous deposits is no criterion, as Scimeca and Dockerty (1955) seem to suggest, whereby the benign or malignant disposition of this lesion can be estimated, since in cases of pseudomyxoma peritonei due to such conditions as mucinous infiltrating carcinoma of the appendix, colon, and rectum, and also of ovarian pseudomucinous cystadenocarcinoma, a clinically malignant course may be associated with difficulty in identifying epithelial elements within the large, firmly or poorly supported, pools of mucus that develop in the intraperitoneal metastases.

On the basis of histological features Woodruff and McDonald (1940) classified appendiceal mucoceles into a small group, which they considered to be adenocarcinoma in situ, and a much larger group described as simple, non-neoplastic, cystic dilatation of the appendix due to overproduction of mucin. These authors claimed that the adenocarcinomatous type of mucocele, by disseminating malignant cells after perforation, was the one likely to lead to a diffuse, progressive, fatal form of pseudomyxoma peritonei; yet in their series of 10 such unruptured mucoceles no case developed this complication. The simple, benign type of cystic appendix was regarded as innocuous since an intractable pseudomyxoma peritonei did not follow leakage of the mucinous contents into the peritoneal cavity. In addition, Woodruff and McDonald recognized transitional stages between these two forms of mucocele, and further postulated that the so-called adenocarcinomatous variant resulted from malignant change affecting the epithelium of the simple lesion.

The so-called 'adenocarcinomatous mucocele', in Woodruff and McDonald's series, was usually smaller than the benign mucocele, and the present writers consider it not unlikely that the former type of lesion, despite the papillary arrangement of its single-layered or pseudostratified hyperplastic epithelium, sometimes represents but an early stage in the formation of the latter. Hyperplastic and hypertrophic cuboidal or columnar actively mucin-secreting cells are a feature of the inchoative phases of mucocele formation (Carleton, 1955), and these cells are sometimes disposed in irregular, papillary fashion both in human lesions (*Fig.* 192) and in experimentally induced mucoceles in rabbits (Rubnitz and Hermann, 1943; Cheng, 1949). In man this type of epithelium may be present before there is any marked dilatation of the appendix, at a stage when the muscularis is thickened. The histological appearances of a mucocele, however, are not always related to its size; nevertheless, in spontaneously occurring large mucoceles the epithelial elements tend to be obliterated, often entirely, and the muscle wall markedly attenuated and completely replaced by fibrous connective tissue.

The theoretical possibility, however, exists whereby the epithelial lining of a mucocele may acquire, either *ab initio* (Scimeca and Dockerty, 1955) or secondarily (Waugh and Findlay, 1937; Woodruff and McDonald, 1940), a neoplastic character. Indeed, Scimeca and Dockerty suggest that it is the active proliferation of a papillary mucus-secreting carcinoma in situ which initiates the distension of the appendix. Yet it is debatable whether such papillary lesions are truly carcinomatous in nature, since mucoceles described as malignant, because of their atypical hyperplastic epithelia, seldom resemble early papillary adenocarcinomata of the colonic type (Uihlein and McDonald, 1943) or develop either clinical or morphological features suggesting an infiltrating and metastasizing propensity. Even when a mucocele exhibiting focal or diffuse papilliferous changes is associated with pseudomyxoma peritonei, intramural invasion by epithelial elements is absent and dissemination is not only dependent on rupture of the cystic lesion but is confined to the peritoneal cavity. Certainly in the instance described in this communication, apart from the carcinoid tumour, no evidence was observed of any other infiltrating neoplastic process in the numerous sections prepared from many different areas of the mucocele and remnant of the appendiceal stump.

In contrast, the established mucinous adenocarcinoma of the appendix, as in the cases described by Lesnick and Miller (1949) and Ryan, Beahrs, Woolner, and Bartholomew (1957), is an infiltrating growth, spreading directly into the submucosa, muscularis propria, and, through the serosa, into the adjacent fat. When such a tumour gives rise to pseudomucinous intraperitoneal deposits, metastases usually are already present in the regional lymphnodes.

The development of pseudomyxoma peritonei from an appendiceal mucocele seems to depend, as D'Aunoy and Fine (1934), Michaelson (1931), Jeffries (1932), Weaver (1937), and Willis (1952) maintain, on whether the lining and the contents, at the time of rupture of the cyst, contain any epithelial elements viable enough to suffer implantation on to the peritoneal surfaces. Thereafter these cells behave abnormally and proliferate as markedly active mucin-secreting structures. Such properties, possibly imparted to the cells within the mucocele as a result of continued protracted obstruction, are reminiscent of neoplastic attributes, since the hyperplastic spilt cells, in their new environment, appear to have acquired an increased capacity for mucin secretion and a malignant-like disposition. The relationship

of these cells to others of undoubted malignant character remains, as pointed out by Chaffee and LeGrand (1942), uncertain and undetermined.

Experimental work, largely carried out on rabbits, has not clarified the pathogenesis of pseudomyxoma peritonei of appendiceal origin in man. The initial work of Rubnitz and his co-workers (Grodinsky and Rubnitz, 1941) seemed to support the cellular theory, since they claimed that when fluid from pseudomyxoma peritonei, obtained from the cœlomic cavity of one rabbit, was deprived of cells by passage through a Seitz-filter and subsequently injected into the peritoneal cavity of another rabbit, pseudomyxoma peritonei did not develop in the recipient animal: only when the cellular elements had not been eliminated could this condition be induced by the intracœlomic injections of the contents of mucoceles or the emulsions of peritoneal mucinous deposits. Later, however, as a result of further experimental work, Rubnitz and Hermann (1943) concluded that it was the mucoid, not the cellular, element which was responsible for some of the intraperitoneal masses in pseudomyxoma peritonei.

Other authors also, notably Trotter (1910), Cheng (1949), Carleton (1955), and Elliot (1957), have challenged the view that the intraperitoneal gelatinous masses arise from the transplantation of viable appendiceal mucosal cells and have proposed, instead, a serosal theory which postulates that pseudomyxoma peritonei represents a type of foreign-body peritonitis occasioned by the irritating and stimulating effect of the thick mucoid material extruded on the cœlomic mesothelium.

Cheng was largely influenced by the difficulty in establishing with certainty the identity of epithelial-like elements included within the peritoneal masses in pseudomyxoma peritonei and by the failure in his experiments on rabbits to produce mucin from punched-out appendiceal mucosa implanted on the peritoneum. He was impressed also by the ease with which these autografts were engulfed and sealed off by fibrous tissue.

In Cheng's experiments it is doubtful whether the epithelial elements of the rabbit's appendix had been subjected to the effects of pressure for a sufficiently prolonged interval of time to become altered by the effects of continued appendiceal obstruction. Following complete or incomplete occlusion of the human appendix a metaplastic reaction takes place whereby nearly all the mucosal cells are transformed into hypersecreting mucinous elements (*Fig.* 191). Even in the ileostomy syndrome, wherein ordinarily only partial obstruction of the ileal lumen exists, nearly all the epithelial cells are transmuted into ballooned, markedly distended goblet cells. If then, as in Cheng's experiments, the implanted appendiceal epithelial cells had not been altered into very active mucus-secreting forms, their failure to produce mucin on peritoneal implantation is readily understood.

The vermiform appendices of rabbit and man are not strictly comparable functionally or morphologically. This viscus in *Lepus* is easily distended, whereas this organ in man, because of the much greater thickness of its muscularis, is able to withstand more effectively greater intraluminal pressures. Mucin is extruded into the cœlomic cavity readily and relatively soon after appendiceal ligation in the case of the rabbit; in contrast, pseudomyxoma peritonei following obstruction of this organ in man, as pointed out by Rubnitz and Hermann, occurs rarely and only after a considerable time has elapsed.

Cheng (1949) was aware that the non-cellular serosal inflammatory theory of pseudomyxoma peritonei, before it could be completely accepted, required some explanation to account for the vast amount of mucus accumulated, in many cases, within the peritoneal cavity. He imagined that there was a continuous passage of mucus into the abdominal cavity from actively secreting appendiceal mucosal cells. Carleton (1955), too, believed that the establishment of such a fistula might well be a critical factor responsible for determining whether a mucocele would give rise to pseudomyxoma peritonei. Despite the improbability of such a fistula, Carleton further suggested that rupture of a mucocele when lined by a hyperplastic epithelium would enhance the establishment of this type of connexion between the appendiceal lumen and the cœlomic cavity.

A serosal theory based on such a doubtful and improbable mechanism does not explain satisfactorily the failure of the peritoneal pseudomyxomatous deposits to regress, in certain cases, once the offending mucocele has been removed. The suggestion that in these instances, in which lesions progress and become diffuse, the serosal cells have undergone a metaplastic reaction whereby actively mucin-secreting cells are produced, also lacks substantiation. Moreover the histological features of the intraperitoneal deposits in pseudomyxoma peritonei in man differ markedly from those induced in the rabbit. In the case of the latter, as Cheng pointed out, there is evidence of vigorous organization and the exudate contains only a small amount of mucin. Pseudomyxomatous deposits in man show little evidence of cellular infiltration, much viscid mucus, and a variable number of epithelial elements.

A fundamental problem in the pathogenesis of pseudomyxoma peritonei of appendiceal origin concerns the nature of the cellular elements contained within the intraperitoneal gelatinous masses. Protagonists of the serosal theory postulate a mesothelial derivation for these cells; they point out the capacity of such cells to adopt a columnar morphology, stressing that any resemblance to the mucosal cells of the appendix is coincidental and of no histogenetic significance.

As far as the case described above is concerned, it is considered that the epithelial-like cells, present within the peritoneal masses removed at operation and in the ascitic fluid aspirated at intervals following the initial operation, are of appendiceal origin and that they in large measure produced the mucus which has progressively distended the patient's abdomen. This conclusion is suggested by the number of Kulschitsky cells (identified by their argentaffin and diazo reactions) found among acinar and other epithelial-like structures within the gelatinous deposits and exudate (*Fig.* 190). It is realized that the mere presence of argentaffin cells is not an absolute criterion of the endodermal nature of the epithelial elements, for the possibility exists, as in certain pseudomucinous cystadenomata, that the cœlomic epithelium may be competent to differentiate such

cells; yet, because of the distribution, morphology, and situation of such cells within the intraperitoneal epithelial-like elements, it is more likely that their presence connotes structures of intestinal origin.

Certain instances of pseudomyxoma peritonei, occurring as a consequence of the rupture of an appendiceal mucocele, pursue a benign clinical course, for the removal of the perforated cystic appendix is followed by a prompt regression of the intraperitoneal pseudomucinous material (Wilson, 1912; Woodruff and McDonald, 1940; and others). Such a pattern of behaviour is more suggestive of the absence of viable epithelial cells in the extruded cystic contents rather than the failure, as Carleton (1955) maintains, of the torn appendix to form a fistula opening into the peritoneal cavity. As in the cases of Woodruff and McDonald, the peritoneal mesothelium can deal successfully with spilt mucin, from so-called benign mucoceles without lining, only when this substance does not contain epithelial elements capable of transplantation on the peritoneum.

The continued excretion of 5 H.I.A.A. in excess of normal in the case already described is not easily explained and calls for a brief comment. Whereas it is theoretically possible for carcinoid cells to implant on the peritoneal surface, and in this instance after rupture of the mucocele there was a free access to the peritoneal cavity for carcinoid cells exfoliated from the exposed argentiffinoma, nevertheless no such argentiffinomatous tissue was found either in the intraperitoneal masses or in the ascitic fluid aspirated subsequently.

Appendiceal carcinoid tumours, because of their early removal, metastasize only very uncommonly and it is unlikely that the excess of 5 H.I.A.A. in the urine is associated with secondary deposits of argentiffinomatous tissue in the liver. The diarrhœa has abated completely and other features of the carcinoid syndrome have not been exhibited by the patient.

SUMMARY

A case of diffuse, progressive pseudomyxoma peritonei of appendiceal origin in a male has been described. The obstructing agent initiating mucocele formation was a carcinoid tumour (argentaffinoma). This neoplasm, by infiltrating and thereby weakening the wall of the distended viscus, facilitated the rupture of the mucocele and the development of the ensuing peritoneal, pseudomucinous complication.

The pathogenesis of appendiceal mucocele formation and of pseudomyxoma peritonei is discussed; and evidence is presented in support of the theory which postulates that the epithelial-like elements in the latter condition are derivatives of the mucosa of the cystic appendix.

REFERENCES

CARLETON, C. C. (1955), *Arch. Path.* (*Lab. Med.*), **60**, 39.
CASTLE, O. (1915), *Ann. Surg.*, **61**, 582.
CHAFFEE, J. S., and LE GRAND, R. H. (1942), *Arch. Surg., Chicago*, **45**, 55.
CHENG, K-K. (1949), *J. Path. Bact.*, **61**, 217.
COLLINS, D. C. (1955), *Surg. Gynec. Obstet.*, **101**, 437.
D'AUNOY, R., and FINE, A. (1934), *Amer. J. Cancer*, **22**, 59.
ELLIOT, C. E. (1957), *Brit. J. Surg.*, **45**, 15.
EVANS, R. WINSTON (1956), *Histological Appearances of Tumours*, p. 459. Edinburgh: E. & S. Livingstone.
GRODINSKY, M., and RUBNITZ, A. S. (1941), *Surg. Gynec. Obstet.*, **73**, 345.
JEFFRIES, J. W. (1932), *Ann. Surg.*, **96**, 215.
LESNICK, G., and MILLER, D. (1949), *Cancer*, **2**, 18.
MCCORMICK, W. F. (1957), *Arch. Path.* (*Lab. Med.*), **64**, 686.
MICHAELSON, E. (1931), *Acta chir. scand.*, **68**, 37.
MUIR, J. B. G. (1931), *Lancet*, **1**, 131.
PHEMISTER, D. B. (1915), *J. Amer. med. Ass.*, **64**, 1835.
RUBNITZ, A. S., and HERMANN, H. T. (1943), *Arch. Path.* (*Lab. Med.*), **43**, 297.
RYAN, R. F., BEAHRS, O. H., WOOLNER, L. B., and BARTHOLOMEW, L. G. (1957), *Surg. Clin. N. Amer.*, **37**, 1029.
SCIMECA, W. B., and DOCKERTY, M. B. (1955), *Proc. Mayo Clin.*, **30**, 527.
SHEMILT, P. (1949), *Brit. J. Surg.*, **37**, 118.
TIMONEY, F. X. (1944), *Amer. J. Surg.*, **64**, 417.
TOPPING, M. H. (1928), *Calif. West. Med.*, **29**, 186, quoted by WAUGH, T. R., and FINDLAY, D. (1937).
TROTTER, W. (1910), *Brit. med. J.*, **1**, 687.
UIHLEIN, A., and MCDONALD, J. R. (1943), *Surg. Gynec. Obstet.*, **76**, 711.
UNGER, H. M., and PARADNY, R. (1956), *Ann. Surg.*, **143**, 280.
WAUGH, T. R., and FINDLAY, D. (1937), *Amer. J. Surg.*, **37**, 518.
WEAVER (1937), *Ibid.*, **36**, 523.
WELLS, A. Q. (1937), *Brit. J. Surg.*, **24**, 766.
WILLIS, R. A. (1952), *Spread of Tumours in the Human Body*, 2nd ed., pp. 49, 54. London: Butterworth.
WILSON, R. R. (1950), *Brit. J. Surg.*, **38**, 65.
WILSON, T. (1912), *Lancet*, **2**, 1496.
WOODRUFF, R., and MCDONALD, J. R. (1940), *Surg. Gynec. Obstet.*, **71**, 750.

LINDAU'S DISEASE IN A SOUTH AFRICAN FAMILY

A REPORT ON THREE FURTHER CASES

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LINDAU's disease in a South African family was described by Bird and Krynauw (1953). Since that time 3 other members of the same family have undergone craniotomy for Lindau's disease in the Department of Neurosurgery of the Johannesburg General Hospital, making a total now of 8 in all who have undergone operation (*Fig.* 193 D).

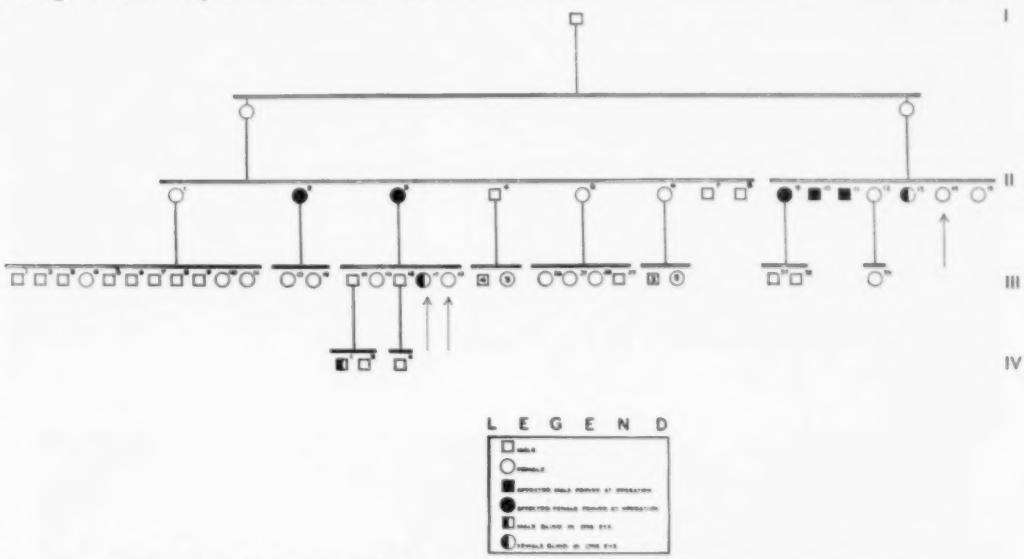

FIG. 193.—Pedigree of a South African family. Those marked with arrows are the three recent cases here reported.

These further cases are now reported, partly because of their number, and partly because improved techniques of investigation, notably vertebral angiography, have assisted in a more precise pre-operative assessment.

Case 6.—The first case, the sixth of the series, was Mrs. M. S. vR., aged 28 years (II^{14} on family tree). She is a half-sister of *Case* 5 reported in the first paper. One month prior to admission she started vomiting, and one week later she developed right frontal headaches. The headaches were never suboccipital. She then developed a feeling of lightheadedness and a tendency to fall to the right when walking or turning. Neurological examination was entirely negative. In view of the family history, we admitted her for investigation.

Right carotid percutaneous angiography was entirely normal. By means of compression of the carotid artery above the needle, and with a sphygmomanometer cuff around the right arm, a retrograde flow of the dye was obtained into the vertebral system. The filling was not entirely satisfactory, but in the pictures no obvious abnormality was noted.

Lumbar puncture pressure was 100 mm. of water, and the cerebrospinal fluid was normal, except for total protein of 60 mg./100 ml.

Air encephalography was attempted on two occasions, without any filling of the ventricular system being obtained. Resort was then made to ventriculography. Bifrontal burr-holes were made, and a catheter introduced into the frontal horn of the left lateral ventricle. Air replacement was performed. The radiographs showed the ventricular system to be normal in size and position. Myodil was then introduced through the catheter. By suitable positioning of the head, and under radiological control, the myodil was induced to flow into the fourth ventricle. The X-ray plates show this ventricle to be markedly displaced from the left towards the right side (*Figs.* 194, 195).

A diagnosis of a space-occupying lesion in the left cerebellar hemisphere was made. At operation a cystic expansion was seen superficially placed in the mid portion of the left cerebellar hemisphere. Twenty c.c. of thick yellow fluid were aspirated. A small red nubbin of tumour was then seen to be lying superficially within the cystic cavity. The feeding artery and two draining veins were visualized and secured. The solid portion of the tumour was removed *in toto*.

Histological examination of the tissues removed showed presence of hæmangioblastoma (*see Fig.* 200). In some areas the nuclei were very large, hyperchromatic, and showed pleomorphism, suggesting local malignancy.

Case 7.—The second patient was admitted to hospital four months after the previous one. She was Mrs. A. S., aged 26 years, and a niece of Mrs. M. S. vR. Her mother, II^{3} on the family tree, had died shortly after the removal of two solid hæmangioblastomata in the cerebellum. At autopsy her pancreas was found to be cystic, and showed

solid hæmangioblastomata. This was the only fatality in the series of 8 cases.

The present patient is shown on the family tree published previously as III[17], and was reported at that time as being blind in the right eye. Two years prior to her present admission her right eye had been enucleated. She gave a history of headaches and vomiting for one year. For six months there had been a tendency to fall to the right side when she walked. Apart from mild signs of cerebellar disturbance in all four limbs, she showed no other neurological abnormality.

Right vertebral percutaneous angiography was performed under general anæsthetic (*Figs.* 196, 197). The

FIG. 194.—*Case* 6. Ventriculogram with myodil. Lateral view showing myodil in distorted fourth ventricle.

FIG. 195.—*Case* 6. Ventriculogram with myodil, showing displacement of the myodil to the extreme edge of the fourth ventricle by intraventricular tumour.

FIG. 196.—*Case* 7. Right vertebral percutaneous angiography, antero-posterior view. This demonstrates vascular tumour in the right cerebellar hemisphere near the tonsil. Further small vascular tumours can be seen elsewhere in the cerebellum, and another protruding through the foramen magnum, and also the suggestion of small vascular tumours in the occipital lobe.

FIG. 197.—*Case* 7.—Right vertebral percutaneous angiography, lateral view. This clearly shows large and small cerebellar tumours, and another tumour extending through the foramen magnum and just beyond the arch of the atlas.

X-ray pictures demonstrated the presence of a vascular tumour in the right cerebellar hemisphere near the tonsil. Another smaller tumour was seen lower down in the left cerebellar hemisphere, and a third higher up towards the cerebello-pontine angle on the right side. The pictures also showed a large vascular tumour protruding through the foramen magnum to the lower border of the first cervical vertebra. This latter was considered to be a tumour of the medulla. In addition to these tumours, the pictures showed numerous scattered small solid tumours throughout both cerebellar hemispheres.

FIG. 198.—*Case* 8. Right percutaneous vertebral angiography, antero-posterior view, showing solid hæmangioblastoma about 1 cm. in diameter, clearly visible in the right cerebellar hemisphere.

FIG. 199.—*Case* 8. Right percutaneous vertebral angiography, lateral view, showing the hæmangioblastoma lying close to the tentorium cerebelli.

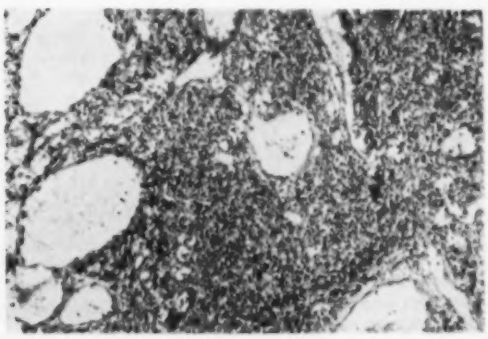

FIG. 200.—*Case* 7. Portion of tumour removed.

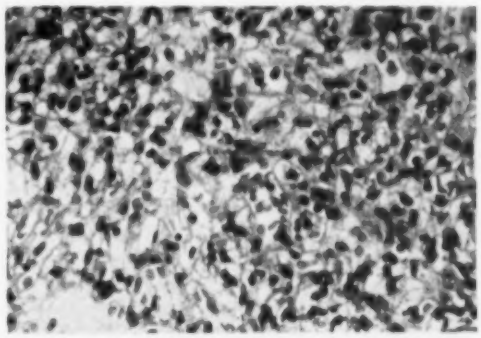

FIG. 201.—*Case* 7. Detail of the structure of part of the tumour removed.

At operation, through a midline, vertical skin incision the bone over both cerebellar hemispheres, the posterior half of the foramen magnum, and the arch of the atlas were removed. The dura over the cerebellum was extremely tense, necessitating tapping of the lateral ventricle via a burr-hole above the lateral sinus on the left side. This relieved the tension in the posterior fossa, and the dura was opened in a cruciate fashion over the cerebellar hemispheres, and the dural opening was extended in the midline over the medulla. The medulla was found to be swollen and distorted by a tumour mass. In the right cerebellar hemisphere a solid tumour about 1½ cm. in diameter was found lying close to the midline. A very large feeding vessel was secured by means of silver clips, and the solid tumour was dissected and removed *in toto*. From the solid part of the tumour a cyst of approximately 10 c.c. capacity extended through the right cerebellar hemisphere towards the cerebello-pontine angle. Removal of this tumour considerably reduced the tension in the posterior fossa, and enabled the tumour in the medulla to be tackled. A needle introduced into the tumour in the medulla showed that there was no cystic component.

A vertical linear incision of approximately 1½ in. in length was made through the middle of the medulla between the lemnisci. At a depth of 1 mm. a vascular, clearly demarcated, red tumour was encountered. A large feeding vessel arising from the left posterior inferior cerebellar artery was ultimately secured, and the entire

tumour was finally removed. A closer scrutiny of the cerebellar hemispheres revealed the presence of numerous small solid tumours, as shown on angiography, and it was considered impractical to attempt removal of all these.

Histological examination of a section of the tumours removed from the cerebellum and medulla showed the typical features of hæmangioblastoma, with closely packed large and small spaces separated by endothelial nuclei and

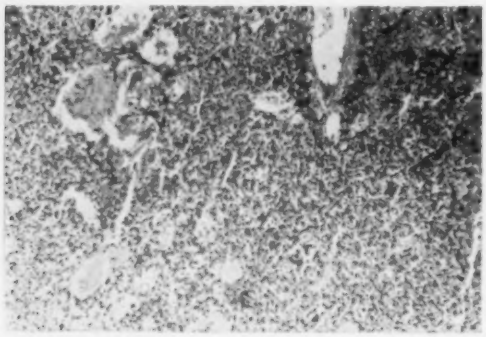

FIG. 202.—*Case* 8. Portion of tumour removed.

foamy phagocytes. The walls of some of the larger spaces were partly hyalinized. There were also areas of hæmorrhage and foci of hæmosiderin deposition. No signs of malignancy were observed in the sections examined (*Figs.* 200, 201).

Mrs. A. S. made a satisfactory post-operative recovery. She became entirely symptom-free. The only abnormalities detectable on neurological examination were joint sense loss in the left hand and loss of vibration appreciation from the clavicles downwards. She was discharged from hospital fifteen days after her operation.

Case 8.—The third patient was Mrs. J. J. T., aged 19 (III[16]), a sister of the previous case (III[17]). Two years previously she had awakened one morning to find that she was blind in her right eye. For four years she had been troubled by occipital headaches and giddiness. This apparently was true vertigo. For two months prior to admission she had been subject to almost daily attacks of vomiting.

Examination showed no evidence of field defect in her left eye. There was no papillœdema or malformation of the retinal vessels. On the right she had no perception of light. The pupil was mid-wide, dilated, and fixed to direct light stimulation, but reacted consensually. Enophthalmos was present on this side.

Neurological examination failed to reveal any abnormal signs except that all four limbs were hypotonic, with reduced reflexes. There was no nystagmus or other signs to suggest cerebellar dysfunction.

Right-sided percutaneous vertebral angiography was performed under general anæsthesia (*Figs.* 198, 199). A solid hæmangioma about 1 cm. in diameter was outlined in the right cerebellar hemispheres, lying superficially near the tentorium.

The presence of this tumour was confirmed at operation. A burr-hole was placed above the lateral ventricle so that the ventricle could be tapped during the operation to regulate the pressure in the posterior fossa, prior to removal of the tumour. This proved to be a solid hæmangioblastoma, with no cystic component. It was removed in its entirety. (*Figs.* 202, 203.)

Vertebral angiography has greatly simplified diagnosis in Lindau's disease. In *Case* 8 it is unlikely that the diagnosis could have been confirmed by any

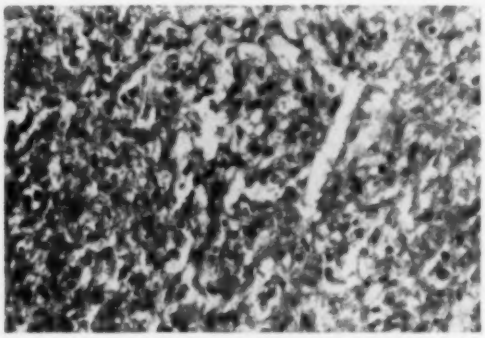

FIG. 203.—*Case* 8. Detail of the structure of part of the tumour removed.

other procedure because of the smallness of the tumour.

In *Case* 7 angiography demonstrated the multiplicity of the tumours, and made it possible to plan the operation in advance, indicating as it did that removal of all the tumours would be impractical.

The remaining case illustrated the value of the opaque medium introduced through the ventricular catheter in outlining a lesion in the posterior fossa, when vertebral angiography proved unsatisfactory.

SUMMARY

A South African family with Lindau's disease transmitted as an autosomal dominant has been described in this and in a previous paper. Eight members have undergone operation for hæmangioblastomata in the cerebellar hemispheres. Improved methods of investigation, particularly vertebral angiography, have greatly assisted in making a more precise diagnosis.

Addendum.—Yet another case (III[18]), a sister of the two patients mentioned above as *Cases* 7 and 8, is reported to be ill, with headache, dizziness, and staggering. She is due for admission to this Unit for investigation.

We wish to thank Dr. N. F. S. Proctor for his assistance in the pathological sections; and Mr. E. R. Rosenberg for carrying out the vertebral angiograms.

REFERENCE

BIRD, A. V., and KRYNAUW, R. A. (1953), *Brit. J. Surg.*, **40**, 433.

METABOLIC DISTURBANCE DUE TO VILLOUS PAPILLOMA OF THE RECTUM

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THE presenting symptom of villous papilloma of the rectum is often mucous discharge. The diagnostic significance of this symptom has been discussed by various authors (Miles, 1939; Gabriel, 1948; Bacon, 1949; Ewing, 1950), but no mention is made of the possible effects of this excessive loss of fluid and electrolytes. We have recently seen 2 patients in whom the loss of fluid from a villous papilloma of the rectum resulted in an electrolyte disturbance. A search of the literature has revealed only 2 other reported cases, and 1 similar case in which severe dehydration occurred owing to a villous papilloma of the gall-bladder (Kerr and Lendrum, 1935).

Fitzgerald (1955) described a woman, aged 57 years, who had had intermittent diarrhœa for two years. One week before admission this became extreme and was accompanied by muscle cramps. On admission she was grossly dehydrated and had a systolic blood-pressure of 60 mm. Hg. She was not thought fit to be moved from the Casualty Department until after 5 pints (2·8 l.) of normal saline had been given. The following day she had greatly improved, after a total of 8 pints (4·5 l.) of normal saline. The plasma electrolytes were then: sodium 128, chloride 92, bicarbonate 11·2, and potassium 4·1 mEq./l., blood-urea 205 mg./100 ml., and the hæmoglobin 120 per cent. She was then given 5 g. of sodium chloride daily by mouth, but twelve days later the plasma-sodium had fallen to 119 mEq./l. The blood-urea was still 65 mg./100 ml. and the potassium 6·6 mEq./l. The salt intake was increased to 15 g. daily and she subsequently had a resection of a villous papilloma of the sigmoid colon.

Frazier (1956) reported a similar case. A 76-year-old man was admitted with a five-week history of diarrhœa and epigastric pain; he was grossly dehydrated and ill. The blood-pressure was 180/100 mm. Hg, the blood-urea nitrogen 145 mg./100 ml. (equivalent to 310 mg. urea/100 ml.), sodium 110 mEq./l., and bicarbonate 27·3 mEq./l. He was thought to have a duodenal ulcer and accordingly was treated with antacids and belladonna. No attempt was made to correct the severe hyponatræmia. His diarrhœa continued and on the fourth day he collapsed. Intravenous fluids and Levarterenol (*L*-noradrenaline) were given, but he died three days later. Post-mortem examination revealed a villous papilloma of the rectum which had not been felt on rectal examination during life.

The first case now reported was in gross electrolyte and fluid imbalance and gravely ill on admission. The second case looked clinically quite well, but her plasma electrolytes were abnormal.

CASE REPORTS

Case 1.—A female, aged 69 years, was admitted with retinal detachment. She was confused, incontinent of fæces and urine, would not eat, and it was difficult to make her drink. After two days she began to vomit and was transferred to a general surgical ward.

ON EXAMINATION.—She was very ill and drowsy, and though she could be roused with difficulty, a history could not be obtained. There was gross dehydration, with a pulse-rate of 100/min. and a blood-pressure of 80/60 mm. Hg. No masses were felt in the abdomen or on rectal examination. There was a profuse discharge of mucus from the rectum, the cause being undetermined at this time.

After a sample of venous blood had been withdrawn for electrolyte estimations, 1½ litres of normal saline was given intravenously in one hour, and this raised the blood-pressure to 115/80 mm. Hg.

Table I.—ELECTROLYTE CONTENT OF MUCUS FROM TWO PATIENTS WITH A VILLOUS PAPILLOMA OF THE RECTUM

(The values for gastro-intestinal secretions are the mean values obtained by Lans, Stein, and Meyer, 1952)

SPECIMEN	Na mEq./l.	Cl mEq./l.	K mEq./l.
Mucus (*Case* 1): on admission	113	120	46
4 days later	105	55	50
Mucus (*Case* 2)	103	99	40
Gastric juice (76 analyses)	56	126	12·6
Small intestinal fluid (12 analyses)	132	68	6·2
Cæcostomy fluid (17 analyses)	69	38	8·2

Investigations.—The plasma-electrolytes were: sodium 99, potassium 2·5, chloride 49, and bicarbonate 16 mEq./l. The hæmoglobin was 110 per cent (16·3 g./100 ml.), the plasma-proteins 8·0 g./100 ml., and the plasma non-protein nitrogen (N.P.N.) 290 mg./100 ml. (corresponding to a blood-urea of more than 500 mg./100 ml.). The urine specific gravity was 1011 and it contained 6 mEq. of sodium, 28 mEq. of potassium, and 4 mEq. of chloride per litre. The electrolyte content of the mucus is shown in *Table I*.

TREATMENT.—During the next fourteen hours she received 1 litre of twice normal saline, 1 litre of normal saline to which had been added 166 mEq. sodium lactate, and 1 litre of Hartman's solution. By the next morning she had passed 2000 ml. of urine. The plasma-sodium was 130, chloride 86, potassium 2·2, and bicarbonate 21 mEq./l. The hæmoglobin had fallen to 80 per cent, the plasma-proteins to 5·1 g./100 ml., and the plasma N.P.N. to 210 mg./100 ml. She was very much better clinically and though still drowsy could be roused easily, but it was four or five days before she became mentally normal. She then gave a history that the diarrhœa had been present for three months.

In view of the very high plasma N.P.N. a high fluid and salt intake was maintained to ensure an adequate diuresis. She continued to pass 2–3 litres of urine daily for four or five days. The excretion of urea amounted to 20–30 g. daily, and on the fifth day of treatment the plasma N.P.N. had fallen to 31 mg./100 ml. This rapid return to normal was related to the small size of the patient, whose normal weight was 7 st. At the same time the potassium deficiency was corrected by giving intravenous

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supplements of 200 mEq. daily. This large dose was given as the combined loss of potassium in the mucus and urine was thought to be about 100 mEq. daily. By the seventh day of treatment the plasma-potassium had risen to 4·3 mEq./l.

Sigmoidoscopy then showed a papillary tumour secreting large quantities of mucus. This was later resected.

Case 2.—A female, aged 71 years, was admitted with a four months' history of passing watery fluid per rectum up to twenty times a day. This fluid discharge was so marked that her own doctor originally referred her to the Genito-Urinary Department as a case of vesicocolic fistula. She felt well in herself and worked daily in her garden.

ON EXAMINATION.—She appeared quite well, and not clinically dehydrated. The abdomen was normal but rectal examination revealed a soft, mobile tumour about the size of a tangerine. On passing a proctoscope, about 50 ml. of clear mucous fluid escaped. Cystoscopy showed a normal bladder and sigmoidoscopy a papilliferous tumour at 10 cm. Biopsy showed this to be a benign papilloma of the rectum.

Investigations.—The plasma-electrolytes were: sodium 132, potassium 2·8, chloride 96 mEq./l.; the plasma N.P.N. was 82 mg./100 ml. (equivalent to a urea concentration of about 120 mg./100 ml.); the plasma-proteins 8·3 g./100 ml., and the hæmoglobin 100 per cent (14·8 g./100 ml.). The urine contained 40 mEq. of sodium, 25 mEq. of potassium, and 36 mEq. of chloride per litre. The electrolyte content of the mucus is shown in *Table I*.

TREATMENT.—She was given a high fluid intake by mouth and 7 g. of sodium chloride and 8 g. of potassium citrate were added daily to the normal hospital diet. Four days later the plasma-sodium was 136, potassium 3·1, and chloride 102 mEq./l. The non-protein nitrogen had fallen to 42 mg./100 ml., plasma-proteins to 7·1 g./100 ml., and hæmoglobin to 90 per cent. Local excision of the tumour was carried out two days later.

DISCUSSION

The clinical picture and the severity of the metabolic upset on admission were very different in these two patients. *Case* 1 was extremely ill and presented a picture similar to that described by Fitzgerald (1955) and Frazier (1956). The severity of the electrolyte disturbance with the extremely low sodium concentration of 99 mEq./l. was only revealed by chemical estimations. The complete diagnosis was not made until the sigmoidoscopy several days later. In *Case* 2 the tumour was easily felt on rectal examination. The patient had no general symptoms and had been gardening up till the day of admission. The plasma-electrolytes were only estimated because of the recent memory of *Case* 1, but the examination revealed low sodium and potassium concentrations and a high non-protein nitrogen.

The amount of mucus secreted by rectal papillomata is variable. In *Case* 2 the volume collected during one 24-hour period in hospital amounted to more than 1 litre. The volume was not measured in *Case* 1, but after rehydration there was a daily difference between fluid intake and urine output of about 1800 ml. Allowing 800 ml./day for loss by evaporation, this suggests a rectal loss of the order of 1 litre daily. The electrolyte content of the mucus in these two patients is shown in *Table I*, together with the average values for other body secretions obtained by Lans, Stein, and Meyer (1952). The electrolyte content of the mucus is relatively high and considerable amounts may be lost if the volume secreted is large. No data are available for the amount of mucus lost in the two previously reported cases, but it appears that Fitzgerald underestimated the loss in his case as the plasma-sodium fell from 128 to 119 mEq./l. during a 12-day period in which the patient was receiving salt supplements.

The development of severe metabolic disturbance in such patients depends on the balance between intake and loss. In the presence of normal intestinal absorption and renal conservation, the average diet contains enough salt and potassium to balance a loss of up to 1 litre of mucus daily. If, however, this balance is disturbed by such factors as diarrhœa, vomiting, abnormal renal function or diminished dietary intake, then rapid depletion will occur which may give rise to a vicious circle of anorexia and vomiting and further loss.

Papilloma of the rectum is an uncommon condition, and metabolic upset of the degree seen in *Case* 1 must be rare. Nevertheless, the possibility is one which should be borne in mind when patients are losing large quantities of mucus, so that any abnormalities may be corrected before surgical treatment is undertaken.

SUMMARY

Two patients are described in whom a mucus secreting papilloma of the rectum caused a disturbance of the body fluids. One was very ill on admission and had a plasma-sodium of 99 mEq./l. The other appeared clinically well and the electrolyte disturbance was only discovered as a result of blood examination.

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REFERENCES

BACON, H. E. (1949), *Anus, Rectum and Sigmoid Colon*. Philadelphia: J. B. Lippincott Co.

EWING, M. R. (1950), *Ann. R. Coll. Surg. Engl.*, **6**, 413.

FITZGERALD, M. G. (1955), *Brit. med. J.*, **1**, 831.

FRAZIER, H. M. (1956), *J. Amer. med. Ass.*, **160**, 774.

GABRIEL, W. B. (1948), *The Principles and Practice of Rectal Surgery*. London: H. K. Lewis & Co. Ltd.

KERR, A. B., and LENDRUM, A. C. (1935), *Brit. J. Surg.*, **23**, 615.

LANS, H. S., STEIN, I. F., and MEYER, K. A. (1952), *Surg. Gynec. Obst.*, **95**, 321.

MILES, W. E. (1939), *Rectal Surgery*. London: Cassell.

POLYA GASTRECTOMY WITH Y ANASTOMOSIS IN THE TREATMENT OF DUODENAL ULCER

EXPERIENCE DURING AN EIGHT-YEAR PERIOD

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In 1951 the Y anastomosis was introduced in the treatment of our cases of duodenal ulcer by Polya gastrectomy. The reason for this, together with the immediate results, were reported in 1953 (Schofield and Anderson).

As the present communication is the sequel to this paper, it is necessary briefly to recapitulate the salient features. Like other surgeons, we had found

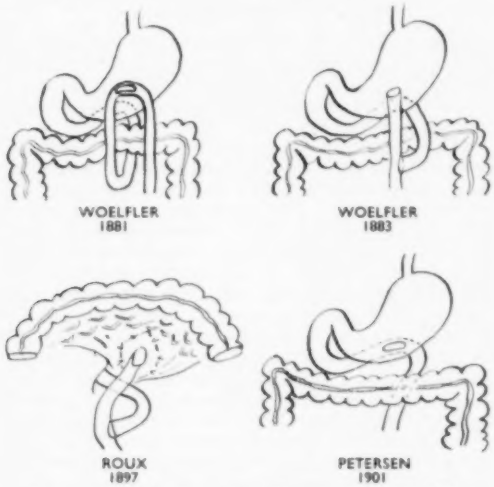

Fig. 204.—Stages in the evolution of gastro-enterostomy. (*After McNeaty, Lichtenstein.*)

that a number of our cases developed the post-gastrectomy syndrome. The term 'post-gastrectomy syndrome' is used in the widest sense, but we were primarily interested in bilious vomiting and excessive loss of weight. It is an unhappy experience to sit face to face with a patient who, having had a Polya gastrectomy performed, nevertheless regrets having submitted to operation on account of severe post-gastrectomy symptoms. Such a condition requires a drastic remedy, and so in 1950 it was decided to anastomose the afferent and efferent loops in 7 post-gastrectomy cases suffering from bilious vomiting. The results were satisfactory, and after further consideration we decided to eliminate the afferent loop altogether by using the Y anastomosis, both in the primary Polya operation for duodenal ulcer and as a conversion operation in cases suffering from severe post-gastrectomy syndrome.

HISTORICAL NOTE (*Fig.* 204)

The first gastro-enterostomy was performed by Anton Wölfler (1850–1917) in Billroth's clinic in Vienna on Sept. 28, 1881. In the years that followed, vicious circle vomiting due to a long proximal loop was a dreaded complication of the operation. It was Wölfler who in 1883 introduced the Y anastomosis (McNealy and Lichtenstein, 1935) in order to prevent this complication which so frequently proved fatal.

Fourteen years later, in 1897, Roux reported having used the Y anastomosis in 29 cases of posterior gastro-enterostomy. Although the Y anastomosis is referred to as 'Roux en Y', Wölfler was its originator, but it was Roux who popularized the operation. The Y anastomosis appears to have been successful in preventing vicious circle vomiting, but anastomotic ulcer frequently followed. Later the Y anastomosis was abandoned for two reasons:—

1. The development of posterior gastro-enterostomy by Courvoisier, von Hacker, and others, resulted in a shortening of the proximal loop, and the work of Petersen, who found that it was possible to anastomose the jejunum to the stomach, close to the duodenojejunal flexure. Petersen's operation was adopted and developed by Mayo in America and by Moynihan in England (McNealy and Lichtenstein, 1935). This resulted in the disappearance of vicious circle vomiting, so that Y anastomosis was no longer necessary.

2. The Y anastomosis was followed by a large number of anastomotic ulcers, and attention was drawn to the fact by the experimental work of Exalto. In 1911 Exalto noticed in the clinic at Utrecht, where a short-loop gastro-enterostomy was performed, that there were very few anastomotic ulcers, but in the Amsterdam clinic, where the Y anastomosis was employed, the incidence of anastomotic ulcer was high (Storer and others, 1952). Exalto thought that this might be due to the fact that in Y anastomosis the alkaline duodenal contents did not come in contact with the anastomosis. He performed the Y operation on dogs by closing the pylorus, dividing the upper jejunum, and anastomosing the distal end of the jejunum to the stomach. The proximal end of the jejunum was implanted into the jejunum. In a high percentage of cases an anastomotic ulcer was produced. Similar results were found in the experimental work of Mann and Williamson and others (Storer and others, 1952).

The Y anastomosis therefore fell into disrepute, and the surgical literature of the last forty years has

contained repeated warnings against its use in the treatment of duodenal ulcer.

Despite these warnings, we felt that the Y anastomosis had been used only before the modern principles governing gastrectomy for duodenal ulcer had been introduced. Until now the Y anastomosis had been employed only in cases of gastro-enterostomy when neither the acid-bearing area nor the pyloric mucosa were removed, and in low partial gastrectomy where a large proportion of the acid-bearing area was left in the gastric remnant.

By the end of 1951 we had performed 31 cases of standard Polya gastrectomy with Y, but there had already been 1 case of anastomotic ulcer (this was one in which Bancroft's modification had been employed, the stomach being divided 2 in. proximal to the pylorus and the mucous membranes dissected out of the funnel of the pylorus; this case will be referred to later). This made us pause in our deliberations, as a result of which we decided to transect the stomach at a higher level, and did so by following the method of measured radical gastrectomy introduced by the late Hedley Visick (1948). At the same time we continued to convert cases of Polya gastrectomy which had developed the post-gastrectomy syndrome.

In an attempt to reduce the recurrent ulcer rate in gastrectomy for duodenal ulcer, Visick introduced the operation of measured radical gastrectomy (M.R.G.). He stated that the recurrent ulcer rate bore an inverse relationship to the level of gastric transection. The recurrent ulcer rate was 5·3 per cent in a "half to two-thirds gastrectomy", 3·7 per cent in "two-thirds to three-quarters gastrectomy", and nil in M.R.G. (*Fig.* 205). In the operation of M.R.G. Visick divided the left gastric artery at its origin from the cœliac axis artery, thus mobilizing the lesser curvature. He divided all but the highest of the vasa brevia, thus mobilizing the fundus. This caused the stomach to change shape by increasing in length and contracting in width, so becoming tubular. This procedure allowed 4–6 in. additional greater curvature to be resected, and the anastomosis could be done with the clamp outside the abdomen. Visick claimed that he was thus able to measure the size of the part left in situ, which is 1½ in. on the lesser curve and 3 in. on the greater curve, that the gastric remnant is extremely devascularized, and that in 98 per cent of the cases permanent achlorhydria results. He reported that in 350 such operations no case of recurrent ulcer resulted, macrocytic anæmia did not occur, and the operative mortality-rate did not increase. Visick's report of 1948 was brought up to date by Pulvertaft (1952) and extended to include the partial gastrectomies done by him from that time until his death in 1949. Pulvertaft confirmed that there had been no case of recurrent ulcer in Visick's series of M.R.G. He also noted that the extent of the resection did not affect the clinical result, but that the weight loss was slightly greater in M.R.G.

FIG. 205.—Incidence of recurrent ulcer in relation to extent of gastrectomy and blood-supply of gastric remnant A, M.R.G. B, "Two-thirds to three-quarters gastrectomy". C, "Half to two-thirds gastrectomy". (*After Visick.*)

THE OPERATIVE TECHNIQUE OF Y ANASTOMOSIS

The technique of this operation has already been described (Schofield and Anderson, 1953), but in the light of experience, however, it has been improved so that a brief description of the operation finally adopted is given (*Fig.* 206).

The operation is performed as for a Polya gastrectomy with division of the gastrocolic omentum along the greater curvature and invagination of the duodenal stump. The thin lesser omentum is divided and the stomach turned upwards, thus exposing the pedicle of the left gastric artery. This artery is divided close to its origin from the cœliac axis artery and doubly ligated. This gives immediate release to the lesser curvature, which is cleaned for the final anastomosis with the jejunum by removal of its veins, after which the raw area is sutured. Attention is then paid to the greater curvature, which has already been partly dealt with, and the left gastro-epiploic artery and all but the highest of the vasa brevia ligated. This gives complete release to the stomach and allows it to be turned over to the left and covered with a warm towel.

The next stage in the operation is the fashioning of the Y jejunal loop. This manœuvre adds about 25 min. to the time of the usual Polya gastrectomy. The jejunum is divided some 12–18 in. below the duodenojejunal flexure. It is unnecessary to ligate the vessels of the mesentery as access can be gained through a bloodless jejunal window, and the widest one is selected. The bowel is divided between a proximal non-crushing clamp and a distal small Payr's crushing clamp, the incision being made flush with the crushing clamp.

A Mikulicz suture is then applied over the Payr's clamp. When the clamp is removed the two ends of the suture are pulled taut and the return suture picks up the peritoneal coat, small bites being taken, thus preventing a bulky head of jejunum. It is a definite improvement in technique, for we have found that if the jejunal head is bulky there is a tendency for it to fall away from the final anastomosis with the gastric remnant.

The proximal jejunum is then sutured to the side of the distal jejunum about 12 in. lower down. A Cawardine clamp is useful as it allows the movement of rotation, thus providing eversion for the posterior peritoneal suture. This completes the fashioning of the Y loop and all that remains is to make the gastro-jejunal anastomosis. As Visick pointed out, the release of the gastric remnant is so complete that the anastomosis can be done outside the abdomen, the stomach being put on the stretch and a gastric clamp applied. This should be applied firmly or some of the stomach may gradually slip back through the clamp, particularly at the greater curvature, thus leaving a larger gastric remnant than was intended. Unfortunately, this happened in one case which was excluded from the high-level series and relegated to the standard-level series. This case has recently developed a recurrent ulcer; this is referred to later. This mistake can be avoided by applying a pair of tissue forceps distal to the gastric clamp at the edge of the greater curvature. A Hoffmeister valve is used solely to prevent the rush of food into the jejunum. For this anastomosis catgut is now used, but in our first 75 cases we used a non-absorbable suture.

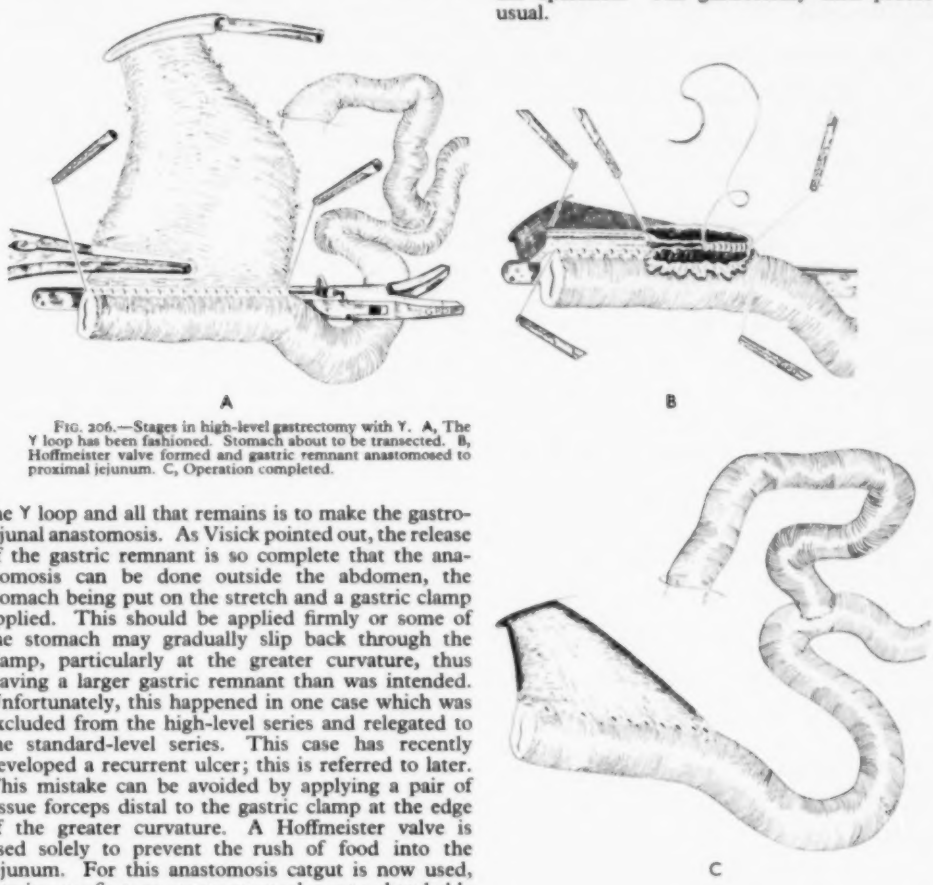

FIG. 206.—Stages in high-level gastrectomy with Y. A, The Y loop has been fashioned. Stomach about to be transected. B, Hoffmeister valve formed and gastric remnant anastomosed to proximal jejunum. C, Operation completed.

Y Conversion of a Polya Gastrectomy for Relief of Post-gastrectomy Syndrome.—The efferent loop from the gastrojejunal anastomosis is easily identified. Usually the first 2 ft. of the efferent loop are thickened and dilated. This may be compensation for loss of gastric reservoir. The afferent loop leading up to the gastrojejunal anastomosis is next identified and divided between clamps close to the stomach. The stomach end is sutured and invaginated. The other end is anastomosed to the side of the efferent loop. This operation is simple and of short duration and compares favourably with the much more difficult operation of conversion to Billroth I.

Y Gastrectomy for Stomal Ulcer following Gastro-enterostomy.—The stomal ulcer having been identified, the afferent and efferent loops of the gastro-enterostomy are divided transversely. The efferent loop is closed with a Mikulicz suture and the afferent loop anastomosed to the side of the efferent loop about 12 in. lower down. In this case the Y anastomosis is fashioned at an early stage in the operation. The gastrectomy then proceeds as usual.

RESULTS

The use of the Y anastomosis does not add to the immediate morbidity or mortality rate of gastrectomy for duodenal ulcer (*see later*, under 'Operative Mortality-rate'). An advantage incidental to the operation is worth mentioning: by deviation of the afferent loop the duodenal contents pass without interruption by the jejunum so that tension in the duodenum is relieved with less likelihood of 'blowing' of the duodenal stump. In our series there was no single case of dramatic rupture of the duodenal stump, but there were 2 cases in which a small quantity of bile escaped from the wound about the seventh day after operation, with no inconvenience to the patient. This adds emphasis to the opinion of G. F. Henson (1955), who states that rupture of the duodenal stump does not necessarily follow

difficult closure, but sometimes easy closure of the stump. He quotes Aird (1949), Wangensteen (1941), and Tanner (1951), who emphasize that distension of the duodenal stump due to obstruction of the afferent loop may be the most important factor in rupture of the duodenal stump.

Mortality-rate.—

1. *Operative.—*

a. Of 205 primary operations for duodenal ulcer, there were 6 deaths following operation. These occurred in the first 102 cases. The causes of death were as follows:—

i. Leakage from the greater curve of the stomach above the suture line.

ii. Injury to the lower end of the common bile-duct.

iii. Necrosis of the gall-bladder.

iv. Pancreatic fistula.

v. Pulmonary embolus.

vi. Acute perforation of the gastric remnant.

There was no case of duodenal leakage. These misfortunes are incidental to any type of Polya gastrectomy, but some could have been avoided by selection of cases.

Illingworth in a series of 200 cases recorded a mortality-rate of 1 per cent in Polya gastrectomy for duodenal ulcer, but admitted that this result had been due, in part at least, to choice of cases. In our series the last 103 consecutive cases, all gastrectomies at the high level, have been selected and the mortality rate has been nil. It would seem, therefore, that if the pitfalls of the 'inoperable' duodenal ulcer are avoided, no extra risk attaches to the high Y gastrectomy operation.

b. Of 9 cases of high gastrectomy with Y anastomosis for recurrent ulcer following gastro-enterostomy, there was 1 post-operative death from pulmonary embolus.

c. There were no deaths in the 14 cases of Y conversion operation.

2. *Late Mortality.*—Two patients died as the result of the development of anastomotic ulcer and details of these cases are given in the paragraph on recurrent ulceration. There are 2 patients who died some time after their operation. One of these died at another hospital six months after gastrectomy from acute intestinal obstruction due to an omental band pressing on the ileum. The other patient belonged to the Y conversion group and left the district, but committed suicide. When last seen by us he was doing well. Investigation has shown that his suicide was not connected with his operation, but was due to domestic complications.

ASSESSMENT OF LATE RESULTS

A 'follow-up' investigation was carried out by one of us (P. H. D.) on a series of 176 cases of planned operation for duodenal ulcer carried out between May, 1951, and December, 1955. The object was to determine the present symptoms, the general state of health, and the incidence of recurrent ulcer in those patients whose operations had been performed from one to five and a half years earlier. For convenience, the question of mortality-rate and recurrent ulcer will be considered in a combined series (228 cases) which includes a further 52 cases operated on since December, 1955.

Of the 'follow-up' series, all were cases of Polya gastrectomy with Y anastomosis. The majority (130) were gastrectomies at a high level: Visick's (1943) M.R.G. A smaller number (32) had gastrectomies with division at the standard level and removal of two-thirds to three-quarters of the stomach. In another small group (14) a Y conversion operation had been performed on patients who already had had standard level gastrectomies. In 7 of the high gastrectomies the operation was performed on patients in whom an earlier gastro-enterostomy for duodenal ulcer had resulted in stomal ulceration. In all, 155 patients were traced (*Table I*); 147 were interviewed and 8 answered a questionnaire by post, 10 of the remainder are known to have died, and 11 could not be traced.

Vomiting and 'Dumping' Symptoms.— The patients who had a Y conversion done some months or years after their gastrectomy were all cases of transection at the standard level which had been followed by bilious vomiting, and most had lost a great deal of weight. Twelve of these patients were interviewed. In 5 of them marked vasomotor symptoms (faintness, sweating, and weakness after meals) had added to their discomforts. The improvement in all was very striking: 11 patients were completely relieved of their symptoms, while the twelfth felt very much better, although there was still a little faintness and regurgitation after meals. All but 3 had a substantial gain in weight and the average weight gain for the whole group was 15 lb.

In the 143 cases investigated in which a primary Y gastrectomy was performed, there was no case of persistent bilious vomiting and no case of troublesome faintness or sweating after meals, although 7 patients mentioned occasional slight regurgitation of food or fluid after meals and 9 patients occasionally had very mild faintness or dizziness after meals which may or may not have been truly vasomotor in origin. In the whole series only 2 patients had any diarrhœa, one of these passing four or five loose stools daily and the other two stools daily.

It seems evident that the Y anastomosis is effective in relieving bilious vomiting and post-prandial vasomotor symptoms when they occur after Polya gastrectomy, and that if it is done at the time of the operation the development of these symptoms can be prevented.

Abdominal Discomfort after Meals.—The only really common symptom in the series was a feeling of uncomfortable fullness after or during meals, and this is, of course, a common symptom after any type of gastrectomy. It was slightly more noticeable in the high gastrectomies than in the standard gastrectomies (including Y conversion). About three-quarters of the patients with each type of operation stated that they were unable to take a big meal without discomfort, while 37 of the 113 high gastrectomy cases (32 per cent) and 9 of the 42 gastrectomies done at the standard level (22 per cent) could not manage an average meal, as taken before their operation or as compared with the meals of other members of their families, without some discomfort (*Table I*). Most of these patients were very little incommoded, and had learned easily to compensate for their small capacity by moderating the size of

their meals or by taking four or five small meals daily, but a few complained of not being able to "eat a square meal".

State of Nutrition.—In assessing their nutritional state, patients were divided into those who had roughly maintained or had increased their weight and those who had lost weight to the extent of at least 10 lb. It was found that 26 out of a total of 143 patients (18 per cent) had lost 10 lb. or more in weight, and this may be compared with the figures published by Ivy, Crossman, and Bachrach (1950), who in an analysis of 864 cases of partial gastrectomy without Y anastomosis found significant loss of weight in 47 per cent. From this it seems likely that the use of the Y anastomosis may limit the tendency to weight loss. There was no difference in the proportion of cases showing loss of weight between the high gastrectomies (17 out of 113 cases) and those with transection at standard level (5 out of 30); and the incidence among female patients was about the same as in the series as a whole. The Y conversion group was of course excluded from this comparison, since this group consisted of patients in whom post-gastrectomy vomiting had already caused much loss of weight. None of the patients could be described as emaciated and there was none suffering from severe lassitude or weakness. Sixteen patients, however, complained of some lassitude, and this had necessitated a change to lighter work in 3 patients. Four others found that they had to curtail spare-time activities, such as gardening, to some extent, but in the remainder the lassitude seemed so slight as to make no appreciable difference to their habits.

All the patients who were interviewed also had an X-ray examination of the chest and no case of pulmonary tuberculosis was found. Five of the male and 10 of the female patients had a hæmoglobin level below 80 per cent (one of the latter had recently been under treatment for menorrhagia). The anæmias were hypochromic in type.

Functional State.—Each case was assessed according to the standards used by Goligher, Moir, and Wrigley (1956) after the recommendations by Visick eight years earlier, and from *Table II* it will be seen that there was little difference between the high and the standard level gastrectomies in this assessment, and that of the whole series 120 out of 155 could be classed as 'excellent' or 'very good'. Two of the cases classed as 'unsatisfactory' were so classed because they had developed anastomotic ulcers, although after they had been treated by a further operation their condition at the time they were seen would have warranted a higher grading. The results were much the same in the small number of women patients as in the group as a whole, and this contrasts with some other series in which women have been found to give poorer results than men after gastrectomy.

Table I.—MAIN SYMPTOMS IN 155 PATIENTS FOLLOWED-UP

	Number Investigated	Loss of Weight	Lassitude	Fullness after Average Meal	Fullness after Large Meal
Measured radical gastrectomy with Y	113	20 (18 per cent)	13 (11 per cent)	37 (32 per cent)	89 (78 per cent)
Standard gastrectomy with Y	30	6 (21 per cent)	3 (7 per cent)	9 (22 per cent)	29 (72 per cent)
Y conversion of standard gastrectomy	12	—			
Totals	155	26	16	46	118

Table II.—FUNCTIONAL ASSESSMENT

	M.R.G. with Y	Standard Operation with Y	Whole Series	Female Patients
Excellent	21	9	30	4
Very good	66	24	90	13
Fair	23	5	28	6
Unsatisfactory	3	4	7	3
Totals	113	42	155	26

Table III.—SHOWING RECURRENT ULCERATION

Type of Operation		No. of Years of Follow-up	No. of Cases	Known Cases of Recurrent Ulcer
Gastrectomy with Y at *standard* level	Primary	8	31	3
	Conversion	7	3	1*
		6	9	0
		5	1	0
		1	1	1*
	Total		45	5
Primary gastrectomy with Y at high level		7	47	1*
		6	24	0
		5	19	0
		4	26	0
		3	27	0
		2	19	0
	Total		162	1
Gastrectomy with Y at high level for stomal ulcer following gastrojejunostomy		7	1	0
		6	2	0
		4	2	1*
		3	1	0
		1	2	0
	Total		8	1
Primary gastrectomy with Y (Bancroft modification)		8	1	1
		7	3	1
	Total		4	2

* Denotes doubtful ulcer, but included in series.

Only 9 patients had failed to return to their previous occupation, and in only 4 of these did the change of work seem definitely attributable to symptoms produced by the operation. After return to work, nearly all cases had a very good attendance record, and the only patients who subsequently lost time from work because of abdominal symptoms were the 2 with recurrent ulcers and 3 others in whom transient attacks of vomiting had necessitated single short periods of observation in hospital. Very few patients had any limitation of social activities: 5 had to limit or give up their gardening (3 because of lassitude and 1 because of abdominal pain when lifting) and 2 others were slightly limited in other ways by lassitude. All the patients seen seemed well pleased with the result of their operations, despite any residual symptoms.

Recurrent Ulceration.—In presenting the rate of recurrent ulceration no excuse is made for including all cases of Y gastrectomy dealt with from May, 1951, to September, 1957, because it is recognized that recurrent ulcer can follow soon after gastrectomy. Thompson (1956) reports that two-thirds of recurrent ulcers developed in his cases within a few months of gastrectomy. Visick (1948) found that in ordinary Polya gastrectomy no recurrent ulcer appeared later than eighteen months. Balint and others (1957) found that the average interval between gastrectomy and operation for recurrent ulcer was three years, and only very rarely occurred after four years. The recurrent ulcers recorded in our series occurred on the average about twelve months after gastrectomy. This is in marked contrast to the time taken for recurrent ulcer to appear after gastroenterostomy.

During a period of six and a half years, 228 cases of duodenal ulcer have been treated by gastrectomy with Y anastomosis. There were 7 deaths following operation and 2 patients have since died from other causes. This leaves a total of 219 cases to be considered for recurrent ulceration. This number is made up as follows:—

It will be seen from *Table III* that there are 9 recurrent ulcers in all. It is proposed immediately to exclude 2 of these cases in which Bancroft's modification was used, and to support this decision by quoting briefly from one of them: This was the case of Mr. P., who in 1952 had a large œdematous duodenal ulcer, and so Bancroft's modification was used with Y gastrectomy. Two years later he was admitted with melæna. Medical treatment failed and he developed considerable pain, with diarrhœa. In May, 1955, a large anastomotic ulcer with a gastrojejunocolic fistula was found at operation. The gastric remnant appeared to be surprisingly large. The ulcer was excised and the stomach transected at a high level, and the efferent loop with its Y anastomosis was joined to the gastric remnant. The middle of the transverse colon was excised and the two ends of the divided colon exteriorized as a double-barrelled colostomy. Before closing the abdomen the 'pyloric knob' was inspected, and it was found easy to excise it and to transect the duodenum below the ulcer. The 'pyloric knob' was sent to the pathologist, who reported that it was lined for at least 2·5 cm. of the specimen with gastric mucosa. The patient did well and is quite free from symptoms.

Thompson (1956) states that the most important local factor in the development of marginal ulcer is the pyloric antrum, and the part it can play in defeating success in gastric surgery cannot be emphasized too strongly. By virtue of its hormone 'gastrin', the antrum has the power of stimulating the fundus of the stomach to secrete acid. In describing Bancroft's modification, he says that the anatomy in these cases is often so distorted that it can be difficult, or even impossible, accurately to define the pylorus, and so antral mucosa may unwittingly be left in the stump on occasion.

In our series of 228 cases, Bancroft's modification was used in 4 (1 standard gastrectomy, 3 high-level gastrectomies), and 2 of these, one in each group, developed recurrent ulcer. Of these 2 recurrent ulcers, the case of Mr. P. has been described above, and the other unfortunately developed a subphrenic abscess and died. It was this case that persuaded us to transect the stomach at the high level. It is considered reasonable, therefore, to exclude these 2 cases, as complete removal of the pyloric mucosa cannot be guaranteed.

There now remain 7 recurrent ulcers, 4 of which are doubtful. One of these belongs to the group of 9 cases in which a high-level gastrectomy with Y was performed for stomal ulcer following gastrojejunostomy. This was a man who, in 1953, was operated on for a large fixed œdematous duodenal ulcer and for which anterior gastrojejunostomy was performed. Nearly three years later he developed recurrent ulcer and a high gastrectomy with Y anastomosis was performed. In April, 1957, there was a suspicion of further recurrent ulcer and as a ventral incisional hernia was repaired, an opportunity was taken of opening the peritoneum and a doubtful scar was seen at the site of gastrojejunal anastomosis, and so vagotomy was performed. This recurrent ulcer is doubtful, but is, nevertheless, included in the series. The patient is well and free from symptoms.

With regard to cases of this type, Visick (1948) has stated that transection of the stomach should occur about 2 in. below the œsophageal opening. Balint and others (1957) state that nothing short of total gastrectomy seems sufficient to cure these "pernicious ulcerators".

With regard to the 6 remaining recurrent ulcers, 5 occurred in standard-level gastrectomy with Y. Two of these cases belong to the Y conversion group and 3 to the primary Y gastrectomy group. The 2 cases in which recurrent ulcer followed Y conversion are both very doubtful, but are included in the series. In one case at operation a doubtful scar was found on the anastomosis, but a vagotomy was performed. It is possible that this condition was present before the Y conversion operation, for in addition to bilious vomiting following gastrectomy, the patient had also complained of pain even before he left the hospital. The other patient had an attack of melæna, but there was no radiological evidence of ulcer. He has remained quite well since, and further operative treatment has not been necessary. This case is further complicated by the fact that this man is a heavy beer drinker.

The 3 patients with recurrent ulcer following primary standard-level Y gastrectomy underwent operation and in each case a large gastric remnant

was found and a higher-level gastrectomy performed. One case died after operation from cardiac failure and another is symptom-free. The third case is an important one because it was intended at the primary operation to perform high-level gastrectomy with Y but, unfortunately, at the end of the operation it was observed and recorded in the operation notes that a larger amount of greater curvature had been left in the gastric remnant than had been intended, and that this case should not be included in the series of high-level gastrectomy with Y. The case was, therefore, relegated to the group of standard-level gastrectomy with Y and has since developed a recurrent ulcer with melæna and pain as the main symptoms. At operation a large recurrent ulcer was found and excised, and it was noted that about 7 in. of greater curvature had been left in the gastric remnant at the first operation. This was due to slipping of the stomach through the gastric clamp, a possibility which has already been referred to in the paragraph on the operation. This case underlines the risk of recurrent ulceration from a standard-level Y gastrectomy.

One patient with recurrent ulceration remains to be discussed and this is the only case occurring in 162 cases of high-level gastrectomy. This was a man who two years after his operation had a mild hæmatemesis and a radiograph queried an anastomotic ulcer. He recovered quickly and has remained at work for four years. He has increased his weight by nearly 2 st. and is a heavy worker, doing ten hours a day. This case is also complicated by the fact that he drinks six pints of beer every evening. He is quite symptom-free and if this patient had a recurrent ulcer he has recovered very quickly from it, but it is, nevertheless, included in the series.

DISCUSSION

We may now consider whether the results so far obtained justify the hopes entertained when one of us (J. E. S.) embarked on this procedure eight years ago.

The results of Y conversion of standard-level gastrectomy for 'dumping' were dramatic and showed how bilious vomiting could be eradicated and how with Y anastomosis the patients increased in weight. As has been noted, this procedure is not safe from recurrent ulceration and it is recommended that vagotomy be undertaken at the same time as the conversion operation. This is not a new idea, for it has been practised by Wells and Johnston (1956) since 1954; and, indeed, was considered in relation to the present series in 1951. It was thought at the time, however, that the addition of vagotomy would cloud the issue. In the light of our experience we now think it would lessen the risks of recurrent ulceration. Similarly, the primary operation with Y at standard level (our first 30 cases, plus 1 case of intended high gastrectomy with Y which was a technical failure) is not safe from recurrent ulceration and there would seem to be no place for this operation unless vagotomy will give the necessary protection. Of the 45 cases of primary and conversion standard-level Y gastrectomies there were 5 recurrent ulcers, although 2 of these were doubtful.

It is, however, with the results of the high-level Y gastrectomy that we are mainly concerned; an operation which aims at a good functional result and freedom from recurrent ulceration. High-level transection of the stomach for duodenal ulcer has been widely criticized. Capper (1956) thought that not more than 70 per cent of the stomach should be removed in duodenal ulcer except in special cases, because it may be followed by serious loss of weight. Welbourn (1953) thought that loss of weight following gastrectomy in general will vary directly with the amount of stomach resected, and that women suffer a greater loss of weight than men when a corresponding amount of stomach is removed. Wells (1954) stated that high gastrectomy as a prophylaxis against stomal ulcer may prove, in terms of nutrition, a high price to pay for this immunity, and, with Welbourn, he thought that the higher the resection the greater the freedom from anastomotic ulcer, but the more probable the development of serious post-gastrectomy syndrome. Johnson (1948, 1954) thinks the degree of weight loss appears to be proportional to the amount of stomach removed. Bearing in mind these criticisms, attention is drawn above to the assessment of our results (P. H. D.), where it will be noted that there was little difference in the functional state and the weight changes between the standard-level and the high-level gastrectomies, and that the results were very much the same in women patients as in the group as a whole. It would seem, therefore, that these criticisms do not find support in our series in which the Y anastomosis was employed.

In this connexion, a recent paper by Balint and Gummer (1958) is relevant. They performed total gastrectomy for 12 cases of benign peptic ulcer, comprising 3 gastric and 9 anastomotic ulcers. Those cases of total gastrectomy in which the Roux en Y reconstruction was used gave the best results. Their nutrition was satisfactory, they could eat a normal amount of food, and maintain their weight.

We stated in our paper in 1953 (Schofield and Anderson) that "if time proves that this form of anastomosis renders the patient more liable to recurrent ulceration, then, however beneficial may be the effects on the 'dumping' syndrome, the operation would have no place in surgery". One cannot, therefore, fail to be impressed by the very low recurrent ulcer rate in the cases of high-level transection.

The operation of high-level gastrectomy with Y must be judged against the background of a number of other surgical procedures devised to obtain improved results in duodenal ulcer. Of these, two should be mentioned as they are in common use: (1) Billroth I gastrectomy; (2) Gastrojejunostomy with vagotomy.

Dissatisfaction has been expressed with the results of the Billroth I operation, and Maloney (1954), at one time one of its most ardent protagonists, now superimposes vagotomy on Billroth I gastrectomy because of a 6 per cent recurrent ulcer rate. Goligher (1956) has abandoned the operation following an investigation of three-year results in which he found a recurrent ulcer rate of 17 per cent. Capper (1956) also recorded a recurrent ulcer rate of 13 per cent.

With regard to vagotomy with gastrojejunostomy, Holt (1956), MacKelvie (1957), Hindmarsh (1957), and others have expressed satisfaction with the results, whilst Burge and Pick (1958) report a recurrent ulcer rate of 4·25 per cent at eight years,

but Henson and Robb (1955) record a recurrent ulcer rate of 12 per cent.

A search of the literature has been made to obtain evidence in support of the operation of high-level gastrectomy with Y for duodenal ulcer, and curiously enough this is produced by Finsterer (1939), who was a great antagonist of the Y loop. Because of its importance the reference is quoted in full:—

"If the gastric secretions have not become neutral, which does not always follow after resection of half of the stomach, and which almost never follows resection of the antrum, the gastrojejunal ulcer will recur after a Y shaped anastomosis; because that part of the anastomotic loop between the gastro-enterostomy and the entero-anastomosis is exposed to the acid contents of the stomach which are first neutralized by bile and duodenal secretions at the entero-anastomosis. Only if the gastric secretions are neutral through extensive resection of the stomach, can one achieve a permanent cure with a Y shaped anastomosis.

"This is well illustrated by two patients, brothers, 42 and 44 years of age, upon whom I operated 19 years ago for gastrojejunal ulcers that developed after gastro-enterostomy. At this time only half of the dilated stomach with the pylorus and the anastomotic loop were removed, and a Y anastomosis performed. After six weeks, pain, hæmorrhage, and heartburn returned. Despite repeated efforts with medical therapy in various institutions there was no improvement. The pain finally became so severe that 6 gr. of morphine administered every 24 hours failed to control it. At the third operation performed upon the brothers in 1921, a large recurrent gastrojejunal ulcer was found penetrating into the pancreas and mesentery of the anastomotic loop, and extending down to the junction with the afferent loop. At that time so large a part of the stomach and also of the Y-shaped anastomosis was resected that only about one-fifth of the normal stomach remained. A new Y-shaped anastomosis was performed. These patients recovered quickly, gaining 15 and 20 kilograms in weight, and have remained free from all symptoms for the past 17 years. Moreover, they observe no diet restrictions and are fully able to work."

In 1951 Tanner stated he had noticed that in the use of the Y anastomosis in total gastrectomy his cases did not develop post-cidal symptoms, and wondered if the anastomosis could be used in partial gastrectomy. He expressed the fear that recurrent ulceration might result. He mentioned that he had performed a case of Y anastomosis in duodenal ulcer with indefinite results.

O'Connell (1955) also noticed the absence of post-gastrectomy syndrome in total gastrectomy with a Y loop, and in 1955 he described a high operation with Y anastomosis in 37 patients operated on for duodenal ulcer since 1953 and with very good results. In 34 of these cases there had been an average gain in weight of 18 lb.

At about the same time that one of us began to use the Y loop, Conyers and Hall were working on similar lines and were employing the Y loop mainly for conversion purposes with dramatic results.

The operations we have described cover a period of eight years and we would hesitate to jump to early conclusions. This period may rightly be considered to be too short for a safe interpretation of the results. A follow-up, however, can be too long delayed, as some patients die from other diseases and others leave the district, so that it is felt that the timing of this paper is justifiable. We suggest that our results show definite trends and encourage us to believe that high-level gastrectomy with Y anastomosis gives freedom from duodenal ulcer pain without the development of the post-gastrectomy syndrome, without an increased risk of recurrent ulceration, and without any increase in the operative mortality. The present series shows that in the majority of cases the nutrition and the general state of health of the patients submitted to this operation are not impaired, and that their capacity for work and recreation is not reduced.

It must be conceded, however, that 90 per cent or more of ordinary Polya gastrectomy patients do well and that most surgeons would not be prepared to undertake a primary high-level gastrectomy with Y despite the results we have recorded. For the relief of the unfortunate 10 per cent a Y conversion operation could be undertaken, but our results show that these cases would be exposed to a higher risk of recurrent ulceration. It remains to be seen whether the addition of vagotomy would provide the necessary protection against recurrent ulceration.

So long as the surgeon is called upon to relieve the pain and complications of duodenal ulcer, an endeavour must be made to produce a standard operation giving the optimum results. This may well come from the simplification of all the many surgical methods which have been advocated, and it is hoped that this paper will contribute something towards this end.

SUMMARY

The history of the Y anastomosis is recorded and reasons advanced for its re-introduction into the surgical treatment of duodenal ulcer.

Operative technique is described and mortality-rate recorded.

An independent assessment of results is given, comparing those of standard and high gastrectomy.

The risk of recurrent ulceration in the use of the Y anastomosis at standard-level Polya gastrectomy for duodenal ulcer is emphasized.

Reference is made to similar work and deductions are made as to the merits of the Y anastomosis in the treatment of duodenal ulcer.

In recording these results, thanks are offered to three former surgical registrars, Mr. P. St. G. Anderson, whose contribution to the early work was invaluable, Mr. G. P. Debenham for the illustrations, and Mr. R. D. Nicholson for his assistance in the follow-up. Thanks are also expressed to the ward and theatre staff and to the Records Department of Victoria Hospital, Swindon, and to the patients who co-operated. Also, one of us (J. E. S.) would like to acknowledge the co-operation and hospitality of Mr. C. N. Pulvertaft and his surgical colleagues at the York County Hospital, who have been working on similar lines.

REFERENCES

AIRD, I. (1949), *A Companion in Surgical Studies*. Edinburgh: E. & S. Livingstone.

BALINT, J. A., COOPER, G. W., PRICE, E. C. V., PULVERTAFT, C. N., and SWYNNERTON, B. F. A. (1957), *Lancet*, **2**, 551.
— — and GUMMER, J. W. P. (1958), *Ibid.*, **1**, 1044.
BURGE, H., and PICK, E. J. (1958), *Brit. med. J.*, **1**, 613.
CAPPER, W. M. (1956), *Proc. R. Soc. Med.*, **49**, 503.
CONYERS and HALL, quoted by PULVERTAFT, C. N. (1954).
FINSTERER, H. (1939), *Surg. Gynec. Obstet.*, **68**, 334.
GOLIGHER, J. C. (1956), *Proc. R. Soc. Med.*, **49**, 510.
— — MOIR, P. J., and WRIGLEY, J. H. (1956), *Lancet*, **1**, 220.
HENSON, G. F. (1955), *Lancet*, **1**, 595.
— — and ROB, M. C. (1955), *Brit. med. J.*, **2**, 588.
HINDMARSH, F. D. (1957), *Lancet*, **1**, 1113.
HOLT, R. L. (1956), *Proc. R. Soc. Med.*, **48**, 501.
ILLINGWORTH, C. F. W. (1953), *Peptic Ulcer*. Edinburgh: E. & S. Livingstone.
IVY, A. G., CROSSMAN, M. I., and BACHRACH, W. H. (1950), *Peptic Ulcer*. London: J. & A. Churchill.
JOHNSON, H. D. (1948), *Post Grad. med. J.*, **24**, 193.
— — (1954), *Ibid.*, **30**, 154.
MACKELVIE, A. A. (1957), *Brit. med. J.*, **1**, 321.
MCNEALY, R. W., and LICHTENSTEIN, M. E. (1935), *Surg. Gynec. Obstet.*, **60**, 1003.
MALONEY, G. E. (1954), *Brit. med. J.*, **1**, 1186.
O'CONNELL, T. C. J. (1955), *Irish J. med. Sci.*, Sixth Series, No. 357, 433.
PULVERTAFT, C. N. (1952), *Lancet*, **1**, 225.
— — (1954), *Ibid.*, **1**, 325 and personal communication.
ROUX, C. (1897), *Rev. Gynéc.*, **1**, 67.
SCHOFIELD, J. E., ANDERSON, P. ST. G. (1953), *Brit. med. J.*, **2**, 598.
STORER, E. H., OBERHELMAN, H. A., jun., WOODWARD, E. R., SMITH, C. A., and DRAGSTEDT, L. R. (1952), *Arch. Surg., Chicago*, **64**, 192.
TANNER, N. C. (1951), *Edinb. med. J.*, **58**, 261.
— — (1954), *Trans. med. Soc. Lond.*, **70**, 141.
THOMPSON, J. E. (1956), *Ann. Surg.*, **143**, 697.
VISICK, A. H. (1948), *Lancet*, **1**, 505.
WANGENSTEEN, O. H. (1941), *Surg. Gynec. Obstet.*, **72**, 257.
WELBOURN, R. B. (1953), quoted by CAPPER, W. M. (1956).
WELLS, C. A. (1954), *Ann. R. Coll. Surg. Engl.*, **16**, 145.
— — and JOHNSTON, J. M. (1956), *Lancet*, **2**, 479.

GAS GANGRENE AS A COMPLICATION OF HÆMATEMESIS

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THE occurrence of visceral infection by *Clostridia* is uncommon. It is occasionally seen following trauma, intestinal perforations, intestinal surgery, gangrenous appendicitis, and puerperal infections.

The association of this type of infection with hæmatemesis does not seem to be a recognized one. The following are the case histories of 3 patients in whom this association was found:

CASE REPORTS

Case 1.—J. F., a male aged 52 years, was admitted in the small hours of the morning of Feb. 6, 1956, following severe hæmatemesis with melæna, twelve and two hours previously. He gave a history of slight dyspepsia for two years, which had become more troublesome during the previous three months. He had noticed that his stools were black on occasions over the last four weeks.

ON EXAMINATION.—He was pale and shocked, with a pulse-rate of 140, blood-pressure 80/40, temperature 97°. He had a little epigastric tenderness, but no guarding, and bowel-sounds were heard. He was treated medically along standard lines with blood transfusion, morphine, etc. His general condition improved on this régime, his blood-pressure rose to about 130–140, but his pulse remained persistently in the region of 120. On the following morning he had a further major hæmorrhage, and complained for the first time of some upper abdominal pain, which gradually became quite severe. At the same time it was found that his epigastric tenderness was rather more marked. The decision to operate was made, and the operation commenced at midday on Feb. 7, by which time he had become rather hot and flushed, with a temperature of 99·6°, and his pulse was full and bounding at the rate of 120.

AT OPERATION.—He was found to have a simple gastric ulcer, about 3×2 in., penetrating the pancreas. Bleeding was coming from the left gastric artery. A Billroth I type of gastrectomy was performed.

During dissection in the region of the duodenum, a small omental vein was divided. Before it was secured it was noticed that bubbles of gas could be seen running along the vein and issuing with the blood from the cut end. The phenomenon was discussed, but no satisfactory explanation was found at this time.

At the end of the operation the patient's condition was poor. It steadily deteriorated and he died about nine hours later.

POST-MORTEM EXAMINATION.—This was performed on the following morning. By this time the body was bloated, and upon being opened the typical smell of gas gangrene became very apparent. There were numerous bubbles of gas in the retroperitoneum, gut, liver, spleen, lungs, and kidneys. A small area of gangrene of the jejunal mucosa, but no other localized lesion, was found. This area was visible only when the gut was opened. Cultures taken grew *Clostridium welchii*.

Case 2.—E. B., a male aged 76 years, was admitted on the evening of July 14, 1957, following a small hæmatemesis. He gave a history of dyspepsia for two months which had become severe in the previous week, during which time he had noticed black stools.

ON EXAMINATION.—He appeared well preserved for his age and his general condition was good. He had a pulse-rate of 80, blood-pressure of 110/60, temperature 98°. Slight epigastric tenderness without guarding was noted, and his bowel-sounds were present.

He was treated medically and remained in good condition until the following morning, when he had two major bleeds and became very shocked. He improved with blood transfusion, but his pulse thereafter remained at about 130 and he looked more ill than one would have expected. Later in the day he began to complain of quite severe upper abdominal pain, his tenderness became more marked, and there was slight guarding.

It was thought possible that his ulcer may have perforated, and operation was advised. At this stage, he had a peculiar smell, sufficiently different from that of melæna alone to arouse comment.

AT OPERATION (11 p.m., July 15).—Upon opening the abdomen the smell became more marked. There was no free fluid and no perforation. The ulcer was a chronic prepyloric one (subsequently proven simple) and a partial gastrectomy was performed with duodenal closure.

On lifting the omentum to deliver the upper jejunum, a wave of foul smell arose and its origin was disclosed. A loop of jejunum about 12 in. long commencing about 18 in. from the duodenojejunal flexure was gangrenous. The colour was green-black, but peritoneal sheen was still present and the mesenteric vessels were pulsating normally. A diagnosis of infective gangrene was made and the loop excised. End-to-end anastomosis was performed and a Polya-type gastrojejunostomy completed. On opening the resected bowel it was found that the mucosal gangrene extended even farther than was apparent from external inspection.

At the end of the operation the patient's condition was poor. In spite of treatment including anti-gas gangrene serum and antibiotics, he died about five hours later.

POST-MORTEM EXAMINATION.—This showed evidence of cardiac failure and a small unsuspected renal carcinoma. There was no sign of residual clostridial infection.

Microscopical examination of the resected bowel showed an acute inflammatory necrosis of the mucosa with marked dilatation of the vessels in the submucosa. Large numbers of Gram-positive bacilli were present in the necrotic mucosa. Cultures of the bowel produced growth of *Clostridium welchii*.

Case 3.—R. J., a woman aged 65 years, was admitted on July 26, following a moderate hæmatemesis. She gave a history of three years' dyspepsia, and had been an in-patient one month previously with hæmatemesis, which had been treated medically. At that time she was shown to have a duodenal ulcer. She had had rather more pain than usual on the three days before her current admission.

ON EXAMINATION.—She appeared rather old for her age, and was very pale and rather shocked. Her pulse-rate was 96, blood-pressure 100/50, temperature 97°. She had a little tenderness in her right iliac fossa and in both hypochondria, no guarding, and her bowel-sounds were present. Her hæmoglobin at this stage was 28 per cent.

She was treated medically with immediate improvement, but over the next three days had several small bleeds. Her blood-pressure and pulse-rate fluctuated considerably, the latter usually being above 100. Her temperature rose above 98° on one occasion only. There was no change in her abdominal signs throughout.

The decision to operate was made on July 29.

AT OPERATION.—Upon opening the abdomen a little free bile-stained fluid was found and a peculiar smell was commented upon. There was a penetrating duodenal ulcer and the bleeding had occurred from the gastro-duodenal artery. There was a considerable amount of retroperitoneal oedema. During the dissection it was discovered that the gastric mucosa was black and necrotic. This was apparent only after the stomach had been sectioned, there being no evidence of it to be seen externally. This necrotic mucosa extended from the pylorus almost to the œsophagus, only the highest part of the fundus escaping. A subtotal gastrectomy with Polya type of anastomosis was performed, a little of the involved mucosa being left in the lesser curve suture line.

The post-operative course was uneventful and when recently seen the patient was very well.

The Specimen.—Sections from the resected stomach show the presence of an acute gastritis with hæmorrhage into the mucosa and submucosa. On the mucosal surface are collections of large Gram-positive bacilli morphologically resembling *Clostridium welchii*. This was subsequently confirmed by culture.

DISCUSSION

Since it is well established that *Clostridia* are inhabitants of the normal human gastro-intestinal tract, and that *Clostridium welchii* are uniformly present in human fæces, it is surprising that infection is so uncommon.

For infection to occur there must be: (1) a portal of entry; and (2) anaerobic conditions suitable for multiplication within the tissues.

In these cases no obvious portal of entry was found. Although each had a chronic peptic ulcer, in *Cases* 1 and 2 the small bowel was primarily involved and even in *Case* 3 the ulcer itself and its immediate surroundings had escaped. One can only assume that invasion occurred via some minor abrasions or perhaps from the depths of a crypt.

The growth of *Clostridia* in the tissues is possible only under conditions of lowered oxygen tension. Usually this is initiated by local trauma, chemical damage, the presence of foreign material, or other pathogenic organisms. In none of these three cases was there evidence of any such a state. There was, however, the common factor of severe and repeated hæmatemesis, and presumably the resulting circulatory depression and lowered hæmoglobin concentration would produce the conditions favoured by *Clostridia*.

Although a pre-operative diagnosis of clostridial infection was not made in these cases, there were several unusual features which are worthy of comment.

Upper abdominal pain and tenderness were outstanding in *Cases* 1 and 2, although much less obvious in *Case* 3. All three had a persistent tachycardia, out of proportion to their hæmorrhagic shock. *Case* 1 showed definite evidence of a febrile illness in the immediate pre-operative period, with his flushed appearance, full rapid pulse, and pyrexia. Unfortunately there is no record of a pre-operative temperature recording in *Case* 2, but since at the end of the operation his temperature was 100·4°, it is likely that it was raised. Perhaps the most characteristic feature of all was the smell, obvious clinically in *Case* 2 and at operation in *Cases* 2 and 3. This was such that it should be easily recognizable if met with again in the future.

The occurrence of three cases of *Clostridium welchii* infection complicating hæmatemesis, seen in one general surgical unit within a period of eighteen months, suggests that the association is more than coincidental.

SUMMARY

1. Three cases of hæmatemesis complicated by gas gangrene are reported.

2. The conditions leading to clostridial infection are discussed in relation to these cases.

3. It is suggested that the hæmatemesis predisposed to the establishment of the infection.

4. The diagnosis may be suspected if a patient with hæmatemesis has increasing upper abdominal pain and tenderness, persistent tachycardia, a rising temperature, and the characteristic smell.

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BIBLIOGRAPHY

Topley & Wilson's Principles of Bacteriology and Immunity, Rev. WILSON, G. S., and MILES, A. A. (1946). London: Arnold.

A System of Bacteriology, M.R.C. (1931). London: H.M.S.O.

INTESTINAL COMPLICATIONS OF STRANGULATED HERNIA*

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LITTLE is known of the fate of a loop of small intestine replaced within the abdominal cavity at an operation for strangulated hernia, for commonly recovery is uncomplicated. Less commonly a degree of partial intestinal obstruction appears to persist, and a few days pass before function is normal. Rarely a late complication arises and an opportunity is afforded for further examination of the bowel at a second operation or at autopsy.

In the first group it is probable that the œdematous, congested loop and its mesentery return rapidly to a normal condition, and peristalsis is promptly resumed. In those that remain partially obstructed there is a paralytic ileus in the involved segment. In some of these certain elements of the loop—serosa, muscle, submucosa, mucosa, or mesenteric vessels—may have been damaged so extensively that healing is by fibrosis, and the late complications of adhesive obstruction or stenosis arise. Such patients with partial or intermittent obstruction may eventually develop macrocytic anæmia. In still others the wall of the replaced bowel is frankly gangrenous and soon becomes perforated. Six patients in whom such late complications occurred are here described, since they illustrate certain points in the diagnosis and management of these lesions.

That 5 of the 6 patients in whom such late complications occurred came within the personal experience of the author within three years suggests that such lesions are not rare. All of these 6 patients were between 60 and 80 years of age, all except one were female, and all except one had a right femoral hernia.

CASE REPORTS

Case 1.—A woman, aged 67 years, was admitted to a cottage hospital with a strangulated right femoral hernia, but by the time the sac was exposed at operation its contents had become reduced and on opening it no bowel was seen. Repair was carried out, but three days later she had nausea, vomiting, and distension, and was transferred to Cardiff Royal Infirmary. She was dehydrated, ill, and mildly febrile. Abdominal examination revealed central distension and some tenderness in the left iliac fossa. Peristaltic sounds were normal, a straight X-ray examination revealed multiple small-bowel fluid levels, and laparotomy was undertaken. The ileum appeared to be completely divided about 24 in. from the ileocæcal valve, the two ends opening into an abscess cavity walled off by loops of bowel and omentum. Resection and end-to-end anastomosis were carried out and recovery was uneventful.

Case 2.—A woman, aged 62 years, was admitted to Cardiff Royal Infirmary with a strangulated left inguinal hernia which had appeared 24 hours before admission. The swelling partially disappeared during the induction of anæsthesia, and only omentum was present when the sac was opened. A loop lying just within the peritoneal cavity was brought down through the inguinal ring and seen to be normal, and the hernia was repaired. On the fourth day she vomited and had colic; hyperactive peristalsis was heard and X-ray examination showed coils of distended small bowel with fluid levels. At laparotomy, a loop of ileum, which lay only 3 in. from the internal inguinal ring, was acutely kinked and adherent to itself and the sigmoid colon. It was so distorted and necrotic that resection was necessary. The patient recovered.

Case 3.—A woman, aged 73 years, was admitted to Boston City Hospital with colic and vomiting following the appearance of a mass in the right groin 24 hours previously. She had a tender, strangulated right femoral hernia and at operation the sac was empty but ecchymotic; it was thought to be infarcted and that this accounted for the small amount of blood-stained fluid it contained. The hernia was repaired and she recovered, but three weeks later she complained of colic after food. Cholelithiasis was suspected and on cholecystography the gall-bladder did not concentrate the dye. She passed a little blood per rectum; sigmoidoscopy was negative and a barium enema showed only diverticulosis of the colon. Her pain persisted and she was admitted for cholecystectomy eleven months after her first operation. At operation the gall-bladder and bile-ducts were normal. The lower ileum was dilated, and was almost completely obstructed by a fibrous stricture 18 in. from the ileocæcal valve. This area was resected and her recovery was uneventful.

Case 4.—A woman, aged 80 years, was admitted to Cardiff Royal Infirmary with a strangulated right femoral hernia of four days' duration. Under local anæsthesia the sac was exposed through an inguinal incision, and found to contain a loop of small bowel which was congested, but which was judged to be viable and returned to the abdomen. The hernia was repaired, she made a good recovery, and returned home, but was re-admitted eight weeks later with a history of three days' colic and vomiting.

Abdominal examination showed distension, tenderness in the right iliac fossa, and absence of peristaltic sounds. A straight X-ray examination showed distended small bowel and right subphrenic free gas. At laparotomy there was generalized peritonitis, with loops of bowel adherent to the region of the hernial repair. Separation of these revealed that the ileum was obstructed by a tight fibrous stricture, and was perforated just proximal to this point. Resection and end-to-end anastomosis were performed. Convalescence was complicated by dehiscence of the superficial wound layers, and after resuture she developed pulmonary atelectasis and congestive cardiac failure, and died. The specimen showed a fibrous stricture so tight that a probe could not be passed through it; the mucous membrane was absent and the muscle and serosa were replaced by fibrous tissue.

Case 5.—A woman, aged 70 years, had an operation for strangulated right femoral hernia at a cottage hospital; the bowel was judged to be viable. Four days later she was admitted to Cardiff Royal Infirmary with nausea, abdominal colic and distension, and hyperactive peristalsis. The ileum was found to be perforated, with abscess formation and obstruction. After resection of the involved segment recovery was uneventful.

Case 6.—A man, aged 77 years, had an incarcerated right femoral hernia reduced by his doctor. Three days later it again became incarcerated and was reduced. From that time he had pain, vomiting, and constipation, and was admitted to Cardiff Royal Infirmary two days later. At operation under local anæsthesia a strangulated femoral

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hernia was found, the sac containing a knuckle of small bowel which was judged to be viable and was returned to the abdomen after one area had been oversewn. Post-operatively there was diarrhœa and vomiting, and twelve days later a laparotomy revealed that the knuckle was

FIG. 207.—*Case* 6. Knuckle of gangrenous, adherent small bowel. (×⅔.)

gangrenous (*Fig.* 207) and had become adherent to itself and to the peritoneum near the femoral canal. Resection was followed by recovery.

DISCUSSION

History and Aetiology.—The first case of stricture after strangulation described in the English literature was by Thomson (1897), of Edinburgh, who refers in detail to previous reports by Garré (1892) and Maas (1895), but a number of French authors preceded these, Guignard (1846) being the earliest traced.

Thomson's patient, a man aged 31 years, came to him with intestinal obstruction twelve weeks after an operation for strangulated inguinal hernia, and was found to have two strictures corresponding to the constriction rings at the limits of the original strangulated loop. The affected bowel was exteriorized and at a later date resected, with successful restoration of continuity by a Murphy's button.

The commonest site for stricture formation is the ileum; it has been described in the jejunum but not in the colon. Most have occurred after inguinal herniæ, but they have been reported after femoral, umbilical, and incisional herniæ also. The stricture may be annular, single or double, or it may be tubular, representing the whole loop. Barry (1942), reporting 3 cases, describes a tubular stenosis 6 in. in length, which represented an 18-in. loop originally strangulated.

The site of the stricture is often adherent to the parietes, omentum, or nearby loops of bowel. The muscle coats proximal to the obstruction show hypertrophy, the submucosa at the stricture is replaced by dense fibrous tissue, and the mucosa is virtually absent, being replaced by granulation tissue (Barry, 1942). More rarely the mucosa shows patchy attempts at regeneration, with irregular gland formation as in the base of a healing chronic peptic ulcer (Tanner and Bratton, 1943). The area may still show discoloration from old hæmorrhage, and there may be streaks of fibrosis and thrombosed vessels in the mesentery (Konstam, 1948). These findings suggest that the stenosis is due to mesenteric vascular trauma as well as to local ischæmic mural trauma by direct pressure. This is borne out by the occurrence of similar strictures after mesenteric tears, hæmatomata following blunt trauma and in hæmophilia, and after mesenteric embolism (Wangensteen, 1955; Hawkins, 1957). Strictures of similar gross and histological appearance have been produced experimentally in rabbits and in dogs by devascularizing loops of intestine (Maas, 1895; Bost, 1929; Wangensteen, 1955). If stricture formation were due to ischæmia of the bowel wall alone, it should frequently follow the well-known manœuvre of inversion of rings or other areas of doubtful viability, or even occur at the site of an end-to-end anastomosis if a rim of crushed tissue is left in situ, yet this has not been described.

Perforation of strangulated intestine which has been replaced in the abdomen has not commonly been reported, but there appear to be two possible mechanisms. In the first type a gangrenous area, which has formed a Richter's hernia and is usually on the antimesenteric border, or an annular area which has been gripped by the neck of the sac, becomes frankly necrotic and disintegrates. If there has been time for the abnormal area to become walled off before this happens, a localized abscess occurs, as in *Case* 1. In the second type normal bowel perforates just proximal to a stricture, as in *Case* 4. Here there is no area of necrotic tissue to promote a localizing peritoneal response, so that general soiling is likely to occur. Oliver (1949) and Orr (1953) report similar small-bowel perforations proximal to strictures.

The important role of infection in determining whether gangrene or recovery occurs has been demonstrated in rabbits by Davis, Gaster, Marsh, and Pritel (1948). Devascularized segments of bowel which otherwise became gangrenous were protected and recovered when parenteral streptomycin was given. More recently Cohn (1956) prevented gangrene in strangulated small bowel in dogs by using achromycin, given into the lumen through an indwelling tube.

In those patients in whom subacute obstruction is allowed to persist for some time, a further complication may arise. Since Faber (1895) first noted the association between intestinal stenosis and macrocytic anæmia, many examples have been reported. This condition, which may also occur with a gastrocolic fistula, diverticulum, or any defunctioned loop of small intestine, is apparently due to stagnation of bowel contents. A change in bacterial flora follows and the absorption or utilization of the hæmopoietic factor is interfered with (Watson and Witts, 1952). None of our patients had this type of anæmia, but Ginsberg (Ginsberg and Klein, 1928) reported 1 patient who died before the association with his stricture was appreciated.

Clinical Features.—Twenty-three examples of stricture formation following strangulation have been collected from the English literature, and an attempt

has been made to summarize their chief clinical features and to compare them with the 2 cases (*Cases* 3, 4) here described (*Table I*).

Thirteen strictures followed femoral, 10 followed inguinal, and 2 followed incisional herniæ; the ileum was the part of the bowel involved in every case where in the abdomen. A L.C.C. subcommittee (1948) set up to investigate the problem reviewed over 350 cases and found that for an identical condition of the bowel the risk of subsequent gangrene was greater where a long loop was involved; loops of over 15 cm. carried twice the mortality of shorter loops. Absence of

Table I.—SUMMARY OF REPORTED CASES OF STRICTURE

AUTHOR	SEX	AGE	HERNIA	STATUS OF BOWEL	SYMPTOMS IN CONVALESCENCE	TIME INTERVAL	AREA AFFECTED	STRICTURE	TREATMENT	RESULT	REMARKS
Garre (1892)	M.	27	Inguinal	Viable	Colic and bloody diarrhœa	5 wk.	Small intestine	7 cm.	Resection	Recovered	
Maas (1895)	F.	47	Inguinal	Viable	Diarrhœa	16 d.	Small intestine	Ring	Resection	Recovered	
Thomson (1897)	M.	31	Inguinal	Viable	Colic, vomiting, and diarrhœa	12 w.	Small intestine	Two rings	Exteriorization, then resection	Recovered	Murphy's button used
Eising (1927)	F.	34	Incisional	Viable	—	2 mth.	Ileum	2 cm.	Entero-enterostomy	Recovered	
Eising (1927)	F.	56	Femoral	Viable	—	7 mth.	Ileum	Ring	Resection	Recovered	
Ginsberg and Klein (1928)	F.	60	Femoral	Viable	—	2 wk.	Small intestine	5 cm.	Entero-enterostomy	Recovered	
Ginsberg and Klein (1928)	F.	50	Femoral	Doubtful	Colic	5 mth.	Ileum	5 cm.	Entero-enterostomy	Recovered	Richter's hernia
Ginsberg and Klein (1928)	M.	45	Inguinal	Unknown	Colic	12 wk.	Ileum	5 cm.	Entero-enterostomy	Recovered	
Ginsberg and Klein (1928)	F.	45	Inguinal	Viable	—	5 mth.	Ileum	8 cm.	No operation	Died	Macrocytic anæmia
Ginsberg and Klein (1928)	F.	66	Femoral	Viable	Colic	2 mth.	Ileum	35 cm.	Entero-enterostomy	Recovered	Probably regional enteritis
Barry (1942)	M.	32	Inguinal	Viable	Colic, vomiting, and diarrhœa	4 mth.	Ileum	15 cm.	Ileostomy	Died	Peritonitis and pulmonary embolus
Barry (1942)	M.	78	Inguinal	Viable	—	5 wk.	Small intestine	5 cm.	Resection	Recovered	
Barry (1942)	F.	59	Femoral	Viable	Colic and diarrhœa	11 d.	Ileum	3 cm.	Ileostomy	Recovered	
Raw (1943)	F.	62	Femoral	Viable	Colic and vomiting	3 mth.	Ileum	Ring	Entero-enterostomy	Recovered	
Raw (1943)	F.	70	Femoral	Viable	Colic and vomiting	7 mth.	Small intestine	15 cm.	Entero-enterostomy	Recovered	
Tanner and Bratton (1943)	M.	61	Inguinal	Viable	Colic and vomiting	7 mth.	Small intestine	8 cm.	Entero-enterostomy, later resection	Recovered	
Konstam (1948)	M.	69	Inguinal	Viable	Colic and vomiting	4 mth.	Ileum	Segment	Ileocolostomy	Recovered	
Konstam (1948)	M.	60	Femoral	Viable	Colic and diarrhœa	3 wk.	Ileum	5 cm.	Entero-enterostomy	Recovered	
Warren and Cattell (1948)	F.	52	Femoral	—	Diarrhœa	28 mth.	Ileum	3 cm.	Entero-enterostomy	Died	Perforation by Miller-Abbot tube
Warren and Cattell (1948)	F.	68	Inguinal	—	Colic and vomiting	8 mth.	Ileum	5 cm.	Entero-enterostomy	Recovered	
Warren and Cattell (1948)	M.	62	Incisional	—	—	30 mth.	Small intestine	Ring	Entero-enterostomy	Recovered	
Teskey (1956)	F.	62	Femoral	Doubtful	Distension	5 mth.	Ileum	Ring	Entero-enterostomy	Recovered	
Teskey (1956)	F.	58	Femoral	Viable	Colic and vomiting	3 mth.	Ileum	4 cm.	Entero-enterostomy	Recovered	
Present series (1957)	F.	73	Femoral	Not seen	Colic	11 mth.	Ileum	Ring	Resection	Recovered	
Present series (1957)	F.	80	Femoral	Not seen	—	8 wk.	Ileum	Ring	Resection	Died	Dehiscence and cardiac failure

this was specified. They occurred nearly twice as frequently in women as in men, the ages ranging from 27 years to our patient of 80 years. In many of the reports a very precise description is given of the state of the bowel at the original operation, with details of tests used to determine its viability before return to the abdomen. In most cases the ordinary criteria for viability were satisfied, and in only 2 instances was it frankly described as 'doubtful'. The tests commonly employed to determine the viability of a loop such as the retention of peritoneal lustre, improvement in colour, peristalsis, pulsation of the mesenteric vessels, and absence of smell, may still leave the issue in doubt. Even when a satisfactory blood-supply is demonstrated, thrombosis of intramural or mesenteric vessels may proceed after the loop has been replaced mesenteric pulsation in a replaced loop was a particularly bad prognostic sign.

In the 2 cases of stricture here recorded the strangulated bowel was never seen. There is no doubt that, particularly if blood-stained peritoneal fluid is present, when the loop is 'lost' in this way it must be sought and inspected before the operation is concluded. This is the chief argument for the use of McEvedy's (1950) approach, or at least the 'high' inguinal operation, in all cases of *strangulated* femoral hernia. The peritoneal cavity in the region of the hernia, where the 'lost' loop will nearly always be found, is thereby easily inspected and resection, if necessary, is facilitated. The decision to resect bowel is, however, not a light one. Jarboe and Pratt (1947) found that the mortality in a large series of

strangulated femoral herniæ at the Mayo Clinic was 10 per cent following reduction of a healthy loop, and 60 per cent following resection. The mortality was 90 per cent if doubtful bowel was replaced in the abdomen. The deciding factor in mortality was the state of the loop of bowel; the patient's age had no effect on mortality, and should therefore not be made an excuse for the replacement of bowel the viability of which is not absolutely certain.

The non-return of function in the replaced loop may be suggested by certain symptoms during convalescence. Diarrhœa, sometimes bloody, was a feature in a number of patients. More constant were colic, nausea, and vomiting, with distension and borborygmi. These symptoms sometimes progressed until a second operation was carried out at an early stage, or subsided after some days, only to recur at intervals with increasing severity; the time interval between operations varied from 11 days to 14 years (Barry, 1942). A barium small-bowel study, made early in the convalescence of any patient suspected of having such an abnormal segment of bowel, might well show the affected segment, as in Hawkins's (1957) case following mesenteric embolus.

Most of these strictures have been treated by a side-to-side entero-enterostomy; of 14 such, 1 died. One of 6 treated by resection died; 1 of 2 where the ileum was exteriorized died. Both patients who had an entero-enterostomy or an ileostomy which was later resected, recovered; 1 patient died without operation. Since resection appears to carry little greater risk than entero-enterostomy, it should be preferred not only because any patient with a small-bowel bypass may later develop a macrocytic anæmia, but also because it affords an opportunity for the histological exclusion of carcinoid and carcinoma.

The high mortality following replacement of gangrenous bowel has already been stressed. Nine of Jarboe and Pratt's (1947) 10 such cases died, even when exteriorization, entero-enterostomy, or inversion of the gangrenous area had been done. All 3 of the cases recorded by the investigating L.C.C. subcommittee (1948) died. The recovery of our *Case* 1 must be attributed to the localization of the abscess by the peritoneum. Clearly resection is the ideal treatment, but in a very ill patient an enterostomy, with resection at a later date, would probably be advisable.

SUMMARY

The occurrence and aetiology of intestinal stenosis, perforation, and macrocytic anæmia after strangulated hernia are reviewed.

An analysis of the chief clinical features of this type of intestinal stenosis, based on 23 previously recorded cases and 2 further cases, indicates that the condition may be suspected from the characteristic history, and is best treated by resection.

The viability of any strangulated loop ought to be assured before it is returned to the abdomen, or it should be resected. A 'lost' loop must be found and inspected at the primary operation.

REFERENCES

BARRY, H. C. (1942), *Brit. J. Surg.*, **30**, 64.
BOST, T. C. (1929), *Ann. Surg.*, **89**, 218.
COHN, I. (1956), *Ibid.*, **143**, 386.
DAVIS, H. A., GASTER, J., MARSH, R. L., and PRITEL, P. A. (1948), *Surg. Gynec. Obstet.*, **87**, 63.
EISING, E. H. (1927), *Amer. J. Surg.*, **3**, 552.
FABER, K. (1895), *Hospitalstidende*, **3**, 601, quoted by WATSON and WITTS (1952).
GARRÉ, C. (1892), *Beitr. klin. Chir.*, **9**, 187, quoted by THOMSON (1897).
GINSBERG, L., and KLEIN, E. (1928), *Ann. Surg.*, **88**, 204.
GUIGNARD, P. E. (1846), *Thèse de Paris*, **444**, 58.
HAWKINS, C. F. (1957), *Lancet*, **2**, 121.
JARBOE, J. P., and PRATT, J. H. (1947), *Surg. Gynec. Obstet.*, **85**, 185.
KONSTAM, P. (1948), *Lancet*, **2**, 569.
LONDON COUNTY COUNCIL (1948), Surgical Subcommittee of the Clinical Research Committee of the Public Health Department of the London County Council. *Brit. med. J.*, **1**, 43.
MAAS, H. (1895), *Dtsch. med. Wschr.*, **21**, 365, quoted by THOMSON (1897).
MCEVEDY, P. (1950), *Ann. R. Coll. Surg. Engl.*, **7**, 484.
OLIVER, B. H. (1949), *Med. J. Aust.*, **2**, 358.
ORR, J. (1953), *Brit. J. Surg.*, **41**, 219.
RAW, S. C. (1943), *Lancet*, **1**, 460.
TANNER, N. C., and BRATTON, A. B. (1943), *Brit. J. Surg.*, **31**, 88.
TESKEY, L. (1956), *Canad. med. Ass. J.*, **73**, 211.
THOMSON, A. (1897), *Brit. med. J.*, **2**, 950.
WANGENSTEEN, O. H. (1955), *Intestinal Obstructions*, 3rd ed. Springfield, Ill.: Charles C. Thomas.
WARREN, K. W., and CATTELL, R. B. (1948), *Amer. J. Surg.*, **75**, 729.
WATSON, G. M., and WITTS, L. J. (1952), *Brit. med. J.*, **1**, 13.

APPENDICEAL CALCULI

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TRUE stones in the appendix are rare and when encountered at operation are of interest for this reason; of greater importance, however, are the radiological appearances, which are fairly characteristic, and which, if not familiar, may cause difficulty in diagnosis.

Wells (1930) reported a case in which a stone was extruded following drainage of an appendix abscess. Subsequent appendicectomy showed a second stone in the appendix which had been seen on X-ray examination, but was considered to be a calcified mesenteric lymph-node.

Levi (1934) described a case which was suggestive of a stone in the lower pole of the right kidney, and Moloney's (1947) case, having obstructive features, was diagnosed as gall-stone ileus. Prather and Singister (1953) discussed the differential diagnosis from ureteric calculi in several cases.

Felson and Bernhard (1947) were able to collect 100 cases from the literature and added 10 cases of their own.

Among more recent references in the British journals may be mentioned those of Chapple (1951), Clark (1952), and Smith (1954).

This paper reports 2 further cases of appendix calculus and discusses the condition, with particular reference to the radiological diagnosis.

CASE REPORTS

Case 1.—P. S. M., male, aged 22 years, a radio-officer in the Merchant Navy, attended the Dreadnought Seamen's Hospital, Greenwich, because during the previous two years he had had three attacks of pain in the right lower abdomen associated with hæmaturia, frequency, and burning pain on micturition. Each attack had lasted a few days and his health, apart from these episodes, had been excellent.

He was a fit-looking young man and examination revealed no abnormal physical signs. A provisional diagnosis of right ureteric colic probably due to stone was made, and a plain radiograph of the abdomen was taken. This showed a large oval laminated opacity in the right side of the pelvis (*Fig.* 208) and he was admitted for further investigation.

Mid-stream urinary examination revealed a moderate number of red cells, but no other abnormality. Intravenous pyelography showed that the opacity had moved to overlie the sacrum and that it was not in the ureter. The urinary tract appeared to be normal (*Fig.* 209).

In view of the history of hæmaturia it was considered advisable to perform cystoscopy and this showed a normal bladder; a right ureteric catheter passed without difficulty and further radiographs confirmed that the opacity was not related to the ureter and that the right renal pelvis was normal.

FIG. 208.—*Case* 1. Plain radiograph showing laminated oval opacity near right ischial spine.

FIG. 209.—*Case* 1. Intravenous pyelogram showing opacity now overlying the sacrum and not in the ureter.

Rectal examination was negative when the patient was first seen, but when repeated in the ward an extremely mobile, hard mass, about 1 in. in diameter, could be felt in the rectovesical pouch. It could not be felt at each examination.

A diagnosis of appendix calculus was made and appendicectomy advised.

AT OPERATION.—The abdomen was opened through a right lower paramedian incision. A grossly enlarged, free-lying appendix, hanging over the pelvic brim and containing a hard concretion, was found. Appendicectomy was performed. No other abnormality was found in the abdomen, which was then closed.

His recovery from the operation was uneventful.

PATHOLOGY.—The specimen consisted of an appendix 8 cm. long, the proximal portion of which was distended to a diameter of 2·5 cm. over a large calculus. This measured 2 cm. by 1·5 cm. and had an uneven dark-brown surface. It could be cut with a knife, and was seen to be composed of a hard dark-coloured outer shell surrounding a friable lighter coloured centre. The wall of the appendix overlying the calculus was thin, and distal to it the lumen was obliterated. Histological examination showed normal mucosa surrounding the calculus and evidence of old inflammatory changes in the distal part.

Comment.—The patient's symptoms may have been due to involvement of the right ureter by episodes of inflammation in the tip of the appendix, but, alternatively, may have been unconnected with his appendix calculus.

Case 2.—E. N., male, aged 45 years, a stone-mason, was sent into Queen Mary's Hospital, Sidcup, as an 'acute abdomen'. He complained of constant severe abdominal pain which had started in the upper abdomen three days before, but was now generalized. Since the onset of the pain he had vomited anything taken by mouth. Any movement by the patient aggravated the pain. His bowels, which usually were regular, had not acted since

the onset of the pain and he was not passing any flatus. He had no urinary symptoms.

PREVIOUS ILLNESSES.—At the age of 24 he had had a right inguinal herniorrhaphy. Three years before his present illness he had had an attack of severe abdominal pain for which an operation had been performed elsewhere. He had been told that a perforated ulcer was suspected,

FIG. 210.—*Case* 2. Plain radiograph (supine) showing small-bowel gaseous distension and circular laminated opacity in the right side of the pelvis.

but later, having made a good recovery, was informed that no abnormality had been found. From that time he had remained in good health until his present illness.

ON EXAMINATION.—T. 99·4° F., P. 85, R. 25. He was a well-built man, obviously in considerable pain. There was clinical evidence of dehydration and his tongue was dry and thickly coated; there was marked fœtor oris. The abdomen was moderately distended and moved poorly on respiration. Widespread rigidity and tenderness were present, rather more marked in the lower abdomen. Severe rebound tenderness was noted and bowel-sounds were diminished in frequency. Rectal examination revealed tenderness and an ill-defined mass in the pelvis.

A diagnosis of peritonitis, probably due to a perforated appendix, was made, but in view of the previous history it was decided to take pre-operative radiographs of the abdomen.

Investigation.—Plain radiographs of the abdomen in the erect and supine positions showed small bowel gaseous distension with fluid levels, and a circular laminated opacity in the right side of the pelvis (*Fig.* 210).

In the differential diagnosis, appendix calculus and gall-stone ileus were the two conditions seriously considered and the former seemed the more likely.

Operation was advised; intravenous fluids were commenced and a Ryle's tube passed.

AT OPERATION.—Under general anæsthesia a right lower paramedian incision was made and on opening the peritoneum distended loops of small bowel showing peritonitis were seen. A moderate amount of turbid fluid was present. In the pelvis, omentum and adherent loops of ileum surrounded a small collection of thin foul-smelling pus in which lay an acutely inflamed appendix containing a hard concretion; the appendix had perforated near its tip. The pus was aspirated and appendicectomy performed.

A drain was placed in the pelvis and brought out through a stab incision, and the abdomen was closed in layers with drainage of the rectus sheath.

Post-operative ileus persisted for three days, during which time intravenous fluid and gastric suction were continued. A course of terramycin, intramuscularly, was given. He made a good recovery apart from wound infection of minor degree, which soon cleared up.

PATHOLOGY.—The specimen consisted of an appendix 5 cm. long × 2 cm. at its widest part. It contained a stone measuring 2 cm. × 1·5 cm. and was acutely inflamed overlying the stone and distal to it where perforation had occurred. The stone showed the same features as those described in *Case* 1.

DISCUSSION

Various authors have given figures ranging from 0·1 to 3 per cent for the incidence of appendix calculus in appendicectomy specimens. Collins (1955), in a study of the pathology of 50,000 appendices mostly removed by operation, found calcified fæcoliths in 302 instances, an incidence of 0·64 per cent.

In their review, Felson and Bernhard (1947) found that the age and sex incidence were similar to those of acute appendicitis, most cases occurring in the second, third, and fourth decades, and males being affected rather more often than females. Childe (1947) reported 8 cases occurring in children between the ages of 5 and 12 years. In over two-thirds of patients the stone is single (Prather and Singister, 1953), and when multiple two or three stones is the usual number. In one of Childe's cases six calculi were present.

Regarding the formation of these calculi, it was at one time thought that they merely lodged in the appendix, and were derived originally from other sources—for example, swallowed foreign bodies, gall-stones, and enteroliths. However, this seems very improbable because frequently these stones are much larger than the normal appendicular lumen and obstruction of the lumen proximal to the stone is a common finding. It is now accepted that they are formed in the appendix itself. Factors favouring stone formation are partial or intermittent obstruction of the lumen and the presence of inspissated fæcal matter which may irritate the mucosa, causing low-grade inflammation and excessive secretion of mucus. The fæcal matter also acts as a nucleus for the deposition of calcium salts. At any time acute appendicitis is likely to occur and probably does so in most patients before there is sufficient calcification to cast an X-ray shadow. This would explain the rarity of the condition radiologically.

Analysis of appendix calculi has shown that they contain about 25 per cent of calcium phosphate, and that this lies mainly in the outer shell, the centre consisting of organic matter, soaps, and cholesterol.

Clinical Features.—Felson and Bernhard (1947) found that about 90 per cent of the cases they reviewed had presented as acute appendicitis, and that in almost 50 per cent of these perforation had occurred. The remainder had ill-defined abdominal

symptoms, often suggestive of some other condition such as peptic ulcer or ureteric colic.

Radiological Appearances.—The opacity may be seen in any position that the appendix may occupy, which includes most of the abdomen, but the great majority occur within a 15 cm. radius of the mid-point of the right ilium. Whilst usually single, multiple opacities may be seen, in which case they lie in a curve or straight line and not in a bunch like calcified mesenteric glands. The opacity is ovoid or circular and has a fairly regular smooth outline. A diameter of 1–3 cm. is the common size. Lamination is a constant feature in a good radiograph, and the relative translucency of the centre often gives a ring appearance. Mobility may or may not be present, depending on the anatomical site and whether or not previous inflammation has led to fixity.

In considering the differential diagnosis of such an opacity in an abdominal radiograph a long list of conditions could be mentioned, but many of them, such as phleboliths, barium residue, foreign bodies, and calcification in fibroids or ovarian cysts, give rise to no difficulty in practice and will not be further discussed. The conditions which from a review of the literature seem to have caused most difficulty in diagnosis are calcified mesenteric lymph-nodes, ureteric and renal stones, and gall-stones, either in a low-lying gall-bladder or in the small bowel causing gall-stone ileus.

The X-ray appearances of calcified mesenteric lymph-nodes are well known. Typically there is a group of opacities of varying size in the right lower abdominal quadrant and each opacity shows uneven patchy calcification and a rough ill-defined outline. The terms 'fragmented' and 'mulberry-like' aptly describe these features. The smooth outline and lamination of an appendix calculus are not seen, but mobility may be noted.

Ureteric stones are usually smaller than appendix calculi and if large tend to be spindle-shaped, with the long axis lying in the line of the ureter. Lamination is seldom seen nor is a ring appearance, and mobility is not a feature. An I.V.P. or retrograde catheterization will decide the diagnosis in doubtful cases.

Some stones in the right kidney, particularly those in the lower pole, may cause confusion, though the appearances of the stone itself are not those of a typical appendix calculus. Again an I.V.P. or retrograde pyelogram may be necessary before a certain diagnosis can be made.

Gall-stones in a low-lying gall-bladder, when multiple and faceted, are unlikely to cause difficulty, but the solitary gall-stone may give very similar appearances to an appendix calculus, although it tends to be less densely calcified. If the clinical features, a lateral radiograph, and a cholecystogram do not prove helpful, the diagnosis may only be made at laparotomy.

In an acute abdomen of uncertain origin where obstructive features have led to a radiograph being taken, gall-stone ileus would naturally be considered as a diagnosis when such an opacity is seen. A gall-stone obstructing the terminal ileum is usually larger but less densely calcified than an appendix calculus. However, lamination may be seen and mobility noted. The presence of definite faceting is suggestive of a gall-stone, and other stones should be looked for in the region of the gall-bladder or elsewhere in the gut. Consideration of the sex and age of the patient, together with the history and clinical findings, will usually enable a correct diagnosis to be reached.

Barium studies are not of much assistance in the diagnosis because an appendix containing a calculus rarely fills. However, a constant relationship of the stone to the cæcum may be demonstrated and this would be suggestive of an appendix calculus. Most cases can be diagnosed without the aid of this investigation.

Treatment.—When met at operation for acute appendicitis a calculus in no way affects the treatment. When the diagnosis is made by X-ray examination of a doubtful acute abdomen urgent appendicectomy is indicated because of the high incidence of early perforation. If an appendix calculus is found during investigation of ill-defined abdominal symptoms or by chance, early appendicectomy should be advised to forestall the almost certain development of acute appendicitis later.

Conclusions.—In a plain radiograph of the abdomen the presence in the right lower quadrant of a fairly smooth, round or oval, usually single opacity 1–3 cm. in diameter, showing lamination or a ring appearance and which may be mobile, is highly suggestive of an appendix calculus.

The increasing use of a 'scout' film before operation in acute abdominal emergencies adds importance to the recognition of the radiological appearances of appendix calculus.

SUMMARY

The literature is briefly reviewed. Two cases of appendix calculus diagnosed pre-operatively are reported. The aetiology, clinical features, and treatment are discussed and emphasis is laid on the radiological appearances and differential diagnosis.

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REFERENCES

CHAPPLE, C. F. (1951), *Brit. J. Surg.*, **38**, 503.
CHILDE, A. E. (1947), *Amer. J. Roentgenol.*, **58**, 455.
CLARK, L. P. (1952), *Brit. J. Surg.*, **40**, 272.
COLLINS, D. C. (1955), *Surg. Gynec. Obstet.*, **101**, 437.
FELSON, B., and BERNHARD, C. M. (1947), *Radiology*, **49**, 178.
LEVI, D. (1934), *Lancet*, **2**, 653.
MOLONEY, G. F. (1947), *Brit. J. Surg.*, **35**, 212.
PRATHER, G. C., and SINGISTER, J. A. (1953), *J. Urol.*, **69**, 5.
SMITH, S. M. (1954), *Brit. J. Radiol.*, **27**, 315.
WELLS, C. A. (1930), *Brit. med. J.*, **2**, 1041.

PLAIN MUSCLE TUMOURS OF THE RECTUM

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THE purpose of this case report and review is to draw attention to a rare lesion of the rectum to which there are few references in British literature.

CASE REPORT

HISTORY.—A 71-year-old man was admitted to hospital on Feb. 6, 1957, with a three-day history of the passage of bright and also altered blood per rectum. For the previous six months he had experienced increasing constipation and for one week abdominal pain relieved by the passage of flatus and fæces.

ON EXAMINATION.—The only physical signs were found on rectal examination, which revealed a mass on

FIG. 211.—Showing how the tumour is expanding and compressing the rectal wall, with thinning of the mucosa but no actual ulceration. (×9.)

the right side of the rectum occupying the ischiorectal fossa and extending posteriorly into the presacral space. The tumour was about 3 in. in diameter, although one could not reach above it with the examining finger; it was firm and elastic to palpation and the overlying mucous membrane was intact.

PROGRESS.—During the next four days small intermittent blood loss necessitated the transfusion of 1 litre of blood.

The insidious onset of large-bowel obstruction was confirmed by an X-ray examination of the abdomen on Feb. 11. Report (Dr. A. H. Muir): "The films confirm considerable gas distension of the large bowel from the cæcum down to the sigmoid colon."

A decision was made to perform an examination under anæsthesia, to biopsy the lesion, and, in view of the developing obstruction, to perform a laparotomy. However, whilst waiting to go to theatre the patient suddenly collapsed, and that night for the purposes of resuscitation 1 litre of dextran and 1·5 litres of blood were given over a period of about 10 hours.

The following day (Feb. 12) his general condition had improved considerably. Increased abdominal distension showed itself and an attempt was made to relieve this with gastric suction. A large rectal catheter was passed above the growth, allowing the escape of flatus and a considerable amount of altered blood.

It had now become obvious that some emergency procedure would be necessary to control the bleeding and relieve the obstruction.

OPERATION.—Examination under anæsthesia added no further information and owing to the presence of altered blood no satisfactory view could be obtained with the sigmoidoscope.

The patient was placed in the combined Trendelenburg-lithotomy position and the abdomen opened by a lower left paramedian incision. Apart from distension of the small and large bowels, no abnormality was found in the upper abdomen. Simultaneous examination of the pelvis from the abdominal and perineal aspects confirmed the previous clinical findings, but demonstrated that the mass was considerably larger than was thought previously. A combined synchronous excision of the rectum was performed, no technical difficulties being encountered during the operation apart from the bulk of the tumour and marked enlargement and engorgement of the veins encountered from the perineal aspect.

POST-OPERATIVE COURSE.—The post-operative course was complicated by paralytic ileus, which persisted for ten days. Wound healing was slow owing to the patient's poor general condition, but he was discharged home seven weeks after the operation.

The overall blood replacement was 5·5 litres.

He was last seen on April 23, 1959, when there was no sign of recurrence.

PATHOLOGICAL REPORT (Dr. H. Williams).—"Rectum and sigmoid colon 23 cm. from the anal margin, with a large firm mass projecting into the lower part of the rectal lumen 5 × 5 cm. and covered by smooth intact mucosa. There was also a subcutaneous mass 2·5-3·0 cm. attached to its lowest part. From its posterior aspect there was a third mass 6 × 6 cm. in continuity with the other two masses.

"*Microscopy*: The tumour consists of spindle-shaped cells with occasional giant forms. Mitoses are moderately frequent (more than 2 per high-powered field). The tumour is invading the muscle layers of the rectum, but has not penetrated to the mucosal layer, which shows pressure effects only– a leiomyosarcoma. (*Fig.* 211.)

"Six lymph nodes – no growth."

It is interesting to note that no obvious bleeding site was seen.

DISCUSSION

Historical.—The first reported case of successful removal of a plain muscle tumour of the rectum was by Carlier and Espt (1881), who removed a tumour the size of a hen's egg through the anus after ligation and crushing the pedicle. After microscopic study of the sections they concluded: "This tumour is thus a fibroma formed by the muscle-fibres of the body and has developed by hyperplasia of the fibro-cellular tissues which form the rectal walls."

Incidence.—Leiomyomata of the alimentary tract, simple or malignant, are rare tumours. They are 8–9 times more common in stomach than rectum (Golden and Stout, 1941; Anderson, Dockerty, and Buie, 1950) and their overall incidence among rectal tumours is estimated by the same authors as 1 : 2–3000. No attempt has been made here to assess the age or sex incidence, as in such rarity this is of little significance.

Pathology.—Plain muscle tumours of the rectum may arise from the muscle coat, muscularis mucosa, or from the plain muscle of the blood-vessels. They are usually placed low in the rectum and almost

invariably within easy reach of the examining finger. They may be single or multiple, sessile or pedunculated. Their size as reported in the literature varies from a few millimetres to 15 cm. in diameter. According to the study of Anderson, Dockerty, and Buie (1950) based on 10 simple and 10 malignant cases seen at the Mayo Clinic between 1911 and 1946, the malignant ones tend to be larger than the simple, the latter averaging only 1 cm. in diameter.

Ulceration of the overlying mucous membrane is fairly frequent, and Anderson, Dockerty, and Buie (1950) regard this as very suggestive of malignancy, since 5 of their 10 malignant cases were ulcerated, whereas ulceration was absent in their 10 benign ones.

These tumours may undergo all the changes that occur in the corresponding tumours in the uterus, viz., hæmorrhage, cyst formation, necrosis, infection, etc., so that their cut surfaces and histological appearances are quite variable.

The mode of spread is essentially by local invasion; occasionally they metastasize to the liver. We could find no case in the literature where the lymph-nodes were found to be involved in a tumour that had been resected.

Histologically the all-important differentiation of simple from malignant is extremely difficult. Golden and Stout (1941), in a very well-reasoned publication, agree to the suggestion of Ghon and Hintz (1909) of employing the term 'malignant leiomyoma' in preference to 'leiomyosarcoma' on the grounds that "... in the minds of many the word 'sarcoma' suggests a high degree of malignancy which these tumours do not possess". These workers (Golden and Stout, 1941) examined critically 60 cases of plain-muscle tumours from the alimentary tract and retroperitoneal tissues (including 5 from the rectum) and contrasted their clinical behaviour with their histological character. They concluded that the degree of differentiation as shown by myofibrils and the histological invasiveness of these tumours which have no true capsule are not a reliable criterion of malignancy, and suggested that if there were two or more mitotic figures per high-power field, malignancy could be confidently predicted, although the converse of this statement seemed untrue.

Appreciation of these histological difficulties by the surgeon is important, as in many cases the preoperative diagnosis will be made on a biopsy specimen and furnished by a pathologist unfamiliar with these rare growths. A report of 'sarcoma' is likely to suggest a hopeless prognosis, whereas a report of 'simple' is likely to lull one into a false sense of security.

Clinical Picture.—Hunt (1921) listed the mode of presentation in 24 cases of 'myoma' of the rectum in order of frequency as: constipation, hæmorrhage, pain in the perineum, obstruction, rectal irritation, desire to stool, mass in the rectum, tumour known to be present, and an accidental finding. Any of these symptoms points to the necessity of full proctological investigation, including endoscopic examination and biopsy.

Carcinoma of the rectum can usually be differentiated by its greater firmness on palpation, by the 'typical' ulcerated surface, and by the tendency to circumferential spread. Such distinction clinically is perhaps academic, as most cases would be submitted to a biopsy.

Biopsy can have its complications, as shown by ReBell and Hiatt (1954), who described a case in which hæmorrhage and hæmatoma formation occurred after punch biopsy. The bleeding was uncontrolled by packing, and after blood transfusion an emergency excision of the rectum was performed.

The vascularity of these tumours as a group is further appreciated by a case described by McVerry and Levene (1956) in which an emergency colectomy was necessary for hæmorrhage following a barium enema.

Treatment.—

a. Radiotherapy.—Radiotherapy has been tried by a number of surgeons and condemned by all (Hunt, 1921, Rankin and Larson, 1932; Golden and Stout, 1941; Oppenheim and O'Brien, 1950; Anderson, Dockerty, and Buie, 1950).

b. Surgery.—It would appear a simple matter to advise local excision for benign leiomyoma and radical excision of the rectum for malignant ones. However, in view of the difficulties inherent in interpreting any biopsy report, one is forced to rely more on clinical assessment than on the histological report.

Hunt (1921) seems to advocate local excision of these tumours, but of the 20 cases which he found in the literature prior to his own cases, none had been followed up. Of the 4 cases which he records, one had multiple recurrences which failed to disappear after radium, one was partially incontinent, one was found accidentally on histological examination of a supposed inflammatory mass excised from the rectovaginal septum, whilst the fourth was reported satisfactory on discharge from the clinic a short time after operation.

Isolated case reports of apparent successful local removal are to be found. Norbury (1934) reported 1 case, but only a short time had elapsed since operation; the case reported by Ghabrial (1955) followed up for two years was probably a pedunculated tumour.

Bargen and Dixon (1934), Neuman (1952), McEachern and Arata (1953), each reports a case of *two* previous local excisions followed by local recurrences necessitating excision of the rectum. Rankin and Larson (1932) reported 4 cases, in all of which local excision had been done one or more times, and followed by local recurrence. This was also the experience of Golden and Stout (1941) and Anderson, Dockerty, and Buie (1950). We get the impression, on reviewing the literature, that the time interval between successive abortive attempts became much shorter, possibly owing to traumatic stimulation.

Local excision of the plain muscle tumours of the rectum should be restricted to small submucosal tumours or pedunculated ones. This course is justifiable in this group since local clearance is more readily obtained, recurrences are easily found, and no dense fibrous adhesions are formed in the perirectal tissues, so that should further surgery be necessary it is not difficult. All other cases should be treated by excision of the rectum, irrespective of the biopsy report of 'simple' or 'malignant'.

The method of excising the rectum is a matter of individual preference, but the surgeon should ligate the inferior mesenteric vessels early in the procedure to avoid embolic spread to the liver. High ligation of the artery flush with the aorta is scarcely necessary as lymphatic spread is almost non-existent; the surgical emphasis should be on wide local clearance.

Prognosis.—The prognosis is difficult to assess owing to: (1) The small number of cases reported; (2) The inadequate follow-up of these cases; (3) The majority have had poor initial treatment in the form of radium or unwise local excision.

If these tumours are treated on the lines indicated above, the prognosis should be good, because they are essentially 'locally malignant'.

SUMMARY AND CONCLUSIONS

1. A case of malignant leiomyoma of the rectum is reported necessitating an emergency combined synchronous excision of the rectum to control hæmorrhage in the presence of intestinal obstruction.

2. Leiomyomata and malignant leiomyomata of the rectum are rare tumours, the diagnosis of which depends on their clinical characteristics and biopsy.

3. The differentiation of simple from malignant on a biopsy specimen is difficult.

4. The term 'sarcoma' is misleading, since it implies a degree of malignancy which these tumours do not possess.

5. Small submucosal or pedunculated tumours should be excised locally; all others should be treated by excision of the rectum with wide clearance of the growth.

6. The prognosis depends on adequate treatment when first diagnosed.

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REFERENCES

ANDERSON, P. A., DOCKERTY, M. B., and BUIE, L. A. (1950), *Surgery*, **28**, 642.
BARGEN, J. A., and DIXON, C. F. (1934), *Amer. J. dig. Dis.*, **1**, 400.
CARLIER, E., and VANDER ESPT, V. (1881), *J. Med. Chir. Pharm. Brux.*, **72**, 140.
GHABRIAL, F. (1955), *Lancet*, **2**, 325.
GHON and HINTZ (1909), quoted by GOLDEN and STOUT (1941).
GOLDEN, T., and STOUT, A. P. (1941), *Surg. Gynec. Obstet.*, **73**, 784.
HUNT, V. C. (1921), *Ann. Surg.*, **74**, 236.
MCEACHERN, C. G., and ARATA, J. E. (1953), *Arch. Surg., Chicago*, **66**, 388.
MCVERRY, E. A., and LEVENE, M. (1956), *Brit. J. Surg.*, **44**, 189.
NEUMAN, Z. (1952), *Ann. Surg.*, **135**, 426.
NORBURY, L. E. C. (1934), *Proc. R. Soc. Med.*, **27**, 930.
OPPENHEIM, A., and O'BRIEN, J. P. (1950), *Amer. J. Surg.*, **79**, 302.
RANKIN, F. W., and LARSON, L. M. (1932), *Minn. Med.*, **15**, 833.
REBELL, F. G., and HIATT, N. (1954), *Amer. J. Surg.*, N.S., **88**, 746.

SPONTANEOUS INTRAPERITONEAL RUPTURE OF SOLITARY (AMŒBIC) LIVER ABSCESSES

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THE rupture of an amœbic abscess of the liver into the general peritoneal cavity has generally been regarded as a particularly serious complication because of the high mortality associated with its occurrence. Since Hulke (1892) first described such a case treated successfully by operation there have been sporadic reports of other successful cases, which have been reviewed by Biggam and Ragab (1931) and Self (1955). In general, however, most of the reports emphasize the failures of treatment—indeed, Rogers (1922), Manson-Bahr (1943), and DeBakey and Ochsner (1951) have regarded the complication as almost invariably fatal. Following the work of Rogers it is generally accepted that amœbæ gain entrance to the liver through the portal system from the intestine. There, a stage of 'amœbic hepatitis' or miliary necrosis of the liver precedes the formation of a usually single, large, necrotic area with a liquid centre, the 'amœbic abscess'. Rupture of such an abscess into the general peritoneal cavity, therefore, represents a very advanced stage in the natural history of the disease. This paper reviews the clinical manifestations of this complication and reports on 5 cases treated with success by the combined use of surgery, antibiotics, and amœbicidal drugs.

CLINICAL FEATURES

Incidence.—That these 5 consecutive cases were seen in one surgical unit within a period of eighteen months suggests that this condition is not rare in Ceylon. This is probably related not only to the high incidence of the primary intestinal infection in this country (Parkinson, 1944), but also to the lack of effective measures for controlling it.

Sex.—All patients were males, a finding in keeping with the observation that amœbic hepatitis and liver abscesses are most uncommon in the female (Craig, 1944).

Age.—The highest incidence of hepatic infection is in the third, fourth, and fifth decades (Reddy and Thangavelu, 1948; Faust, 1954). All 5 patients were within this age-group.

DIAGNOSIS

The correct diagnosis was made before operation in 2 of these 5 cases. In one of these the patient was receiving a course of emetine injections in the

treatment of amœbic hepatitis. The other cases were diagnosed as generalized peritonitis due to other acute abdominal conditions such as perforated appendicitis or peptic ulcers. The difficulty with correct pre-operative diagnosis has been noted previously (Biggam and Ragab, 1931; Self, 1955). In retrospect, the correct diagnosis could be reached if the following factors are borne in mind:—

A history of dysentery may be completely lacking. Only 1 patient complained of loose stools at the time of admission and the other 4 gave no history of recent bowel upset.

A history of prolonged ill health may also be lacking. The clinical course in this series was remarkably short, with an average duration of about a week prior to the rupture of the abscess. It is, however, probable that the onset was so insidious that the symptoms were neglected for some time before they became insistent.

Abdominal pain is not confined strictly to the right hypochondrium prior to rupture. In all cases the pain was located to the right side or the upper abdomen (epigastrium), and this may be due to enlargement of the liver into the abdominal cavity.

In the acute phase following rupture the temperature is raised, the patient acutely ill, and the abdomen rigid. The last makes palpation of the liver impossible, but liver enlargement is detectable because of diminution of breath-sounds in the lower part of the chest on the right side, increase of the area of liver dullness to percussion, and tenderness in the intercostal spaces of the right side. These features may be confirmed by plain radiographs of the abdomen, which show not only elevation of the diaphragm but sometimes a large (negative) liver shadow.

Special investigations such as examination of the stools for amœbæ and the white-cell count are not helpful.

In the cases of the present series the abscesses were single and located in 4 cases to the right lobe, the commonest site for their occurrence. Two abscesses were found on the inferior surface of the liver near the hepatic flexure of the colon, while the other two were placed anteriorly towards the dome of the liver. The 'pus' or necrotic material contained in these abscesses had a viscid, glairy appearance, yellowish-red to chocolate brown in colour, resembling anchovy sauce, "an appearance so characteristic that it may be considered pathognomonic" (DeBakey and Ochsner, 1951). No amœbæ were demonstrable in this material, which was always found to be sterile. The fluid in the peritoneal cavity was similar in nature, except that it was diluted by the peritoneal exudate. The quantity of fluid removed at operation varied between 300 and 1000 ml.

CASE REPORTS

Case 1.—A farmer, aged 46 years, complained of pain in the right side of his abdomen for nine days. The pain had suddenly increased in severity on the day of admission and was accompanied by nausea but no vomiting or diarrhœa. He had felt feverish in the evenings over the past weeks, but there was no history of dysentery. He had had a period of ill health, with right-sided abdominal pain ten months previously. On examination, he was acutely ill and had a temperature of 101° F. and a pulse-rate of 100. The abdomen was slightly distended, with rigidity of the right side and tenderness maximal to the right of the umbilicus. Rectal examination was negative. A diagnosis of perforative peritonitis was made and the patient prepared for operation.

At laparotomy a ruptured liver abscess was found on the inferior surface of a very enlarged right lobe of the liver. About 400 ml. of thick 'anchovy sauce' material were evacuated from the abscess cavity and peritoneum. The former was drained for 48 hours. Intravenous fluids and gastric suction were continued over the same period. Streptomycin and penicillin were given for 2 days, emetine for 10 days, and chloroquine for 3 weeks.

The white-cell count was 9,600, 80 per cent neutrophils; no amœbæ were found on examination of the stools. The patient became apyrexial after the third day and made an uninterrupted recovery, being discharged from hospital on the fourteenth day without any residual liver enlargement. When seen at a follow-up examination one month later he was free of symptoms.

Case 2.—A labourer, aged 37 years, was admitted to hospital complaining of attacks of pain in the epigastrium of nine days' duration. The pain was sometimes referred to the right shoulder and was associated with fever. Six hours previously he had developed very severe epigastric pain and vomited once. He had a mild diarrhœa on the day of admission and had a non-productive cough for five days. There was no history of dysentery.

On examination, the patient was acutely ill, the temperature being 100° F. and the pulse-rate 104. The abdomen moved little with respiration and there was marked rigidity and tenderness in the epigastrium, particularly on the left side. Rectal examination was negative, and a plain radiograph did not reveal gas under the diaphragm.

A diagnosis of perforated gastric ulcer was made and intravenous fluids and gastric suction were instituted as a preliminary to operation.

Laparotomy revealed a ruptured liver abscess in the posterior part of a much enlarged left lobe of the liver. About 500 ml. of reddish-brown material was removed from the peritoneum and abscess cavity, which was drained for 72 hours. Penicillin and streptomycin were administered for 3 days, emetine for 10 days, and chloroquine for 3 weeks. He was discharged on the eleventh day when there was no detectable enlargement of the liver. The stools were negative for amœbæ on repeated examinations and the white-cell count was 10,200, 82 per cent neutrophils. The 'pus' from the abscess cavity was sterile and contained no amœbæ. At follow-up one month later he was quite well.

Case 3.—The patient, an office assistant, aged 47 years, complained of chills and bouts of perspiration over the past week. He had been admitted to hospital for investigation, and while under observation, he had suddenly developed severe upper abdominal pain and collapsed. His appetite had been poor, but he had no nausea or vomiting. There was no history of diarrhœa or blood and mucus in the stools.

On examination, the patient's general condition was poor, his temperature was 100° F., and the pulse-rate 110. Breath-sounds were diminished on the right side of the chest. The abdomen moved little with respiration and there was board-like rigidity. The whole epigastrium was dull to percussion, although the liver was not palpable. There was tenderness in the rectovesical pouch on rectal examination. A plain radiograph of the abdomen showed elevation of the diaphragm on the right side. A diagnosis of ruptured liver abscess was made and the patient prepared for operation with resuscitative measures.

At operation, the liver was grossly enlarged and there was a small quantity of reddish-brown fluid in the peritoneal cavity. The site of rupture was located with difficulty to the right anterior subphrenic region and the abscess cavity was emptied by compressing the liver from

below. About 1000 ml. of fluid were removed by suction. The abscess cavity and the hepato-renal pouch were drained for 48 hours. He was given penicillin and streptomycin for 48 hours, emetine for 12 days, and chloroquine for 4 weeks. His recovery was delayed by secondary infection of the wound with *Staph. pyogenes*, but on discharge from hospital at the end of four weeks he was quite well, although there was slight residual enlargement of the liver. The stools were negative for amœbæ on repeated examination; the white-cell count was 14,000, 88 per cent neutrophils, and the 'pus' from the abscess cavity was sterile. When seen two months later he was without complaints.

Case 4.—The patient, a male aged 29 years, entered hospital with a complaint of a right-sided abdominal pain of four days' duration. He complained of chills and fever and constipation for two days. The pain had radiated to the right shoulder region at first, and later had become more severe in the central part of the abdomen, finally shifting into the right iliac fossa about 6 hours previously. There was no history of dysentery in the past.

On examination, he was in severe pain, the temperature was 102° F. and the pulse-rate 108. There was rigidity of the right side of the abdomen, with marked tenderness in the right iliac fossa, and there was tenderness also in the rectovesical pouch on rectal examination.

A diagnosis of perforated appendicitis was made.

At laparotomy (Dr. L. Kiriella), a ruptured abscess cavity was found on the inferior border of a very enlarged right lobe of the liver. About 500 ml. of chocolate-coloured necrotic material was removed from the peritoneum and abscess cavity, which was drained with a tube for three days. Penicillin and streptomycin were given for 13 days, emetine for 10 days, and chloroquine for 3 weeks. He made steady progress and was quite well on discharge from hospital on the fourteenth day, except for some residual enlargement of the liver. He did not attend follow-up.

Case 5.—A 23-year-old lorry driver was admitted to hospital with a history of upper abdominal pain radiating to the right shoulder, fever, and a non-productive cough of seven days' duration. One month previously he had had an attack of abdominal pain and diarrhœa; the stools had been blood-stained for a few days. A diagnosis of amœbic hepatitis had been made and he was being treated with aureomycin and emetine. Seven days after admission he was suddenly seized with severe abdominal pain and collapsed. Resuscitative measures had been instituted immediately and he had responded well.

On examination, his general condition was satisfactory, the temperature was subnormal (97·0° F.) and the pulse-rate 98. There was rigidity of the abdomen and the area of liver dullness was increased, although the liver itself was not palpable. There was also marked intercostal tenderness on the right side of the lower part of the chest and the breath-sounds on that side were diminished. Rectal examination was negative. A plain radiograph of the abdomen showed elevation of the diaphragm on the right side and a greatly increased liver shadow. A diagnosis of ruptured liver abscess was made.

At laparotomy, about 300 ml. of free fluid were found in the peritoneal cavity and a ruptured liver abscess was found high up on the anterior aspect of the right lobe of the liver. The 'anchovy sauce' material was removed from the peritoneum and abscess cavity and the latter was drained for 48 hours. Resuscitative measures were continued for a further period and he was treated with penicillin and streptomycin for 7 days, emetine for 10 days, and chloroquine for 3 weeks. He ran an irregular temperature ranging as high as 103° F. for seven days and then remained afebrile till he was discharged on the fourteenth day. On discharge from hospital the liver was not perceptibly enlarged on clinical examination and this was confirmed by radiography.

The white-cell count was 22,000, 73 per cent neutrophils, and the stools were negative for amœbæ on repeated examination. He was without complaints when seen one month later.

TREATMENT

Hitherto several methods have been employed in the treatment of this complication; they include open surgical drainage of the abscess or of the peritoneum, and repeated paracentesis of the abdomen with or without other supportive measures. The cases reported here were treated by a combination of surgery, antibiotics, and amœbicidal drugs.

Following a period of resuscitation with intravenous therapy all these patients were subjected to laparotomy. At operation the fluid in the peritoneum and abscess cavity was removed by suction and dry gauze swabbing and the abscess was drained. Prolonged drainage of the latter was avoided by early removal of the drain (within 48 to 72 hours). Intravenous fluid therapy and gastric suction were continued until bowel-sounds were audible, and antibiotics and amœbicidal therapy instituted immediately after operation. Streptomycin and penicillin in combination were administered for 2–13 days to prevent secondary infection, and emetine hydrochloride (½–1 gr.) given daily for 10–12 days. Chloroquine was given for 3–4 weeks from the time the patient could take food by mouth.

The patient usually ran an irregular pyrexia for 3 to 5 days after operation; this fell to and remained normal after this period except in one case where there was secondary infection of the wound with *Staph. pyogenes*. The liver was not palpable in 3 cases after the fourteenth day, but there was residual enlargement in 1 case. There was no case of amœbic infection of the wound.

It would appear that the factors contributing to the successful management of these cases are:—

Early surgical intervention to remove the necrotic material and fluid from the peritoneum.

Prevention of secondary infection by the use of antibiotics and the avoidance of prolonged drainage of the abscess cavity; the discharge from this is very little after the administration of emetine.

Effective amœbicidal therapy with emetine hydrochloride and chloroquine.

Adequate supportive therapy, i.e., intravenous fluid and gastric suction, especially in the pre-operative and immediate post-operative phases.

There is also the further possibility that these patients presenting in such an advanced stage of the disease have in fact developed some added resistance to the infection, as evinced by their remarkable response to these measures.

SUMMARY

The records of 5 consecutive cases of spontaneous intraperitoneal rupture of solitary (amœbic) liver abscesses are presented.

The clinical features of the condition are discussed and a method of treatment combining surgery, antibiotics, and amœbicidal drugs is described, with a comment on the factors contributing to the successful management of this complication, which has previously been regarded as almost invariably fatal.

I wish to thank Mr. A. R. Anscombe, of St. George's Hospital, London, for his help and criticism in the preparation of this paper; and Dr. N. Bartholomeuz, of the General Hospital, Colombo, Ceylon, for his permission to publish these cases.

REFERENCES

BIGGAM, A. G., and REGAB, A. (1931), *J. trop. Med.*, **34**, 285.
CRAIG, F. G. (1944), *The Etiology, Diagnosis and Treatment of Amebiasis*. Baltimore: The Williams & Wilkins Co.
DEBAKEY, M. E., and OCHSNER, A. (1951), *Surg. Gynec. Obstet.* (Int. Abstr. Surg.), **92**, 209.
FAUST, E. C. (1954), *Amebiasis*. Springfield, Ill.: Charles C. Thomas.
HULKE, J. W. (1892), *Brit. med. J.*, **2**, 1169.
MANSON-BAHR, Sir P. (1943), *The Dysenteric Disorders*. London: Cassell & Co.
PARKINSON, T. (1944), *Lancet*, **1**, 612.
REDDY, D. G., and THANGAVELU, M. (1948), *Ind. med. Gaz.*, **83**, 557.
ROGERS, L. (1922), *Lancet*, **1**, 463.
SELF, J. B. (1955), *Post Grad. med. J.*, **31**, 35.

SHORT NOTES OF RARE OR OBSCURE CASES

SIMULTANEOUS CARCINOMA OF JEJUNUM AND COLON

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PRIMARY carcinoma of the large intestine is not infrequently multiple, and when operating for carcinoma of the rectum or colon, most surgeons take the opportunity to examine the whole of the large bowel. Far less common is the simultaneous presence of primary carcinoma in the large and small intestines. Major (1918) collected 628 cases of multiple malignant tumours, and in only one of these were jejunum and colon the sites involved. It is felt, therefore, that the following case is worthy of record.

CASE REPORT

Mr. R. H., aged 44 years, was admitted to hospital on June 26, 1958, with a 2-year history of tiredness, lassitude, and central abdominal pain. For the past year he had suffered from anæmia for which he had received treatment with iron. Despite a good appetite he had lost weight. He had suffered from nausea and had vomited occasionally.

Eight weeks prior to admission he had developed a new and constant pain in the left side.

Examination revealed a thin pale man with obvious weight loss. The mucous membranes were pale. The

FIG. 212.—Photograph of resected portion of jejunum showing the ulcerating carcinoma.

FIG. 213.—Photograph of resected portion of colon showing the large ulcerated carcinoma.

tongue was clean and moist. In the left hypochondrium was a hard irregular mass 8 cm. in diameter. It appeared to be superficially placed and was fixed. Rectal examination revealed nothing abnormal.

The following investigations were carried out: Hæmoglobin, 7·5 g. per cent; chest radiograph, normal. Barium enema showed obstruction in the transverse colon near the splenic flexure; very little barium passed beyond this. Occult blood was present in the stools.

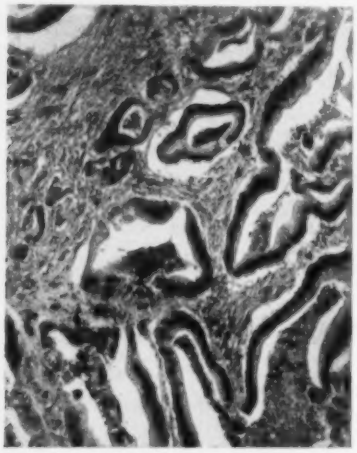

FIG. 214.—Photomicrograph of tumour in the jejunum. Hæmatoxylin and eosin. (× 75.)

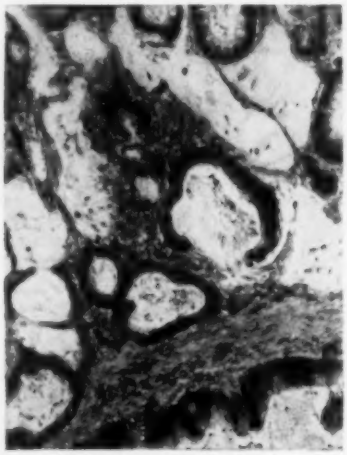

FIG. 215.—Photomicrograph of tumour in the colon. Hæmatoxylin and eosin. (× 75.)

A diagnosis of carcinoma of the transverse colon was made, and after preliminary blood transfusions to correct the anæmia, laparotomy was carried out on July 2, 1958. A large carcinoma was found in the transverse colon 2 in. proximal to the splenic flexure. It was adherent to the peritoneum of the anterior abdominal wall, but apart from this was not attached to any surrounding structure. During the examination of the rest of the abdomen a second tumour was discovered in the jejunum 2 ft. 6 in. from the duodenojejunal flexure. The two tumours were not lying adjacent to each other and did not appear to be connected in any way. They had, in fact, all the appearances of two primary neoplasms. The colonic tumour was the larger. Enlarged lymph-nodes were present in the mesentery from both tumours. The remainder of the gastro-intestinal tract appeared normal. No secondary deposits were palpable in the liver or elsewhere in the abdomen or pelvis. The jejunal tumour was excised, together with an adjacent wedge of mesentery which included the enlarged lymph-nodes. End-to-end anastomosis was then carried out. The colonic tumour was mobilized by resecting a circular area of adherent parietal peritoneum from the abdominal wall. It was removed by left hemicolectomy. The post-operative course was uneventful and the patient was discharged from hospital on July 15, 1958. After convalescence he returned to work as a bus driver and has remained well ever since.

The operation specimen was reported on as follows:

"*Macroscopy.*—Specimen 1 (*Fig.* 212) consists of 13 in. of jejunum, near the centre of which is an ulcerating tumour completely encircling the wall and apparently invading lymph-nodes in the mesentery. The appearances are those of a primary tumour.

"Specimen 2 (*Fig.* 213) consists of 11 in. of the transverse and descending colons. There is an enormous ulcerating tumour which again has the appearance of a primary growth; it has a mucoid appearance, completely encircles the wall of the gut, and is attached to the tissues of the abdominal wall.

"*Histology.*—The tumour of the jejunum (*Fig.* 214) is a well-differentiated adenocarcinoma penetrating muscle to attain the surrounding fat. The adjacent lymph-node is not invaded. The tumour of the colon (*Fig.* 215) is a mucus-secreting adenocarcinoma which has not invaded the mesocolic node but shows an inflammatory reaction. The two tumours are sufficiently similar microscopically to raise some doubt, despite the macroscopic appearances, that they arose independently."

DISCUSSION

Multiple simultaneous cancers are not very uncommon, and often their site and histological structure enable one to be certain that they are, in fact, separate primary growths. In the gastro-intestinal tract, however, it is often more difficult to prove their separate origin, and in the present case the rather similar histological appearances of the two tumours made it necessary to rely largely on indirect evidence to conclude that one was not in fact a metastasis from the other. The possible routes by which such metastasis might have occurred were: (1) Direct extension. (2) Transcœlomic spread. (3) Seeding via the bowel lumen. (4) Lymphatic spread. (5) Blood-stream.

In our opinion all these possibilities were extremely unlikely. Direct extension could be excluded at once as the two tumours were completely separate from one another. Both tumours were comparatively large, and transcœlomic spread would almost certainly have been accompanied by metastases elsewhere in the peritoneal cavity, and furthermore, neither tumour had extended right through to the serosal aspect of the bowel. The implantation in the colonic mucosa of exfoliated cells from the jejunal growth was perhaps less improbable, but against this theory were the facts that the two tumours were a long distance apart, the colonic tumour was considerably larger than the jejunal one, and that this mode of spread is very unusual in bowel neoplasms (Willis, 1952), except where a raw surface such as a suture

line is available for implantation. Lymphatic and hæmatogenous spread could reasonably be excluded in this case by the lack of evidence of spread to the regional lymph-nodes, liver, or elsewhere.

There was no evidence in this case of diffuse polyposis of the intestine, a condition well known to predispose to the development of multiple carcinomata.

This case would seem to underline the importance of examining the whole of the intestinal tract in cases of neoplasm affecting any part of it.

SUMMARY

A case is described of simultaneous carcinomata of jejunum and transverse colon. The reasons for considering these to be two primary tumours are discussed.

Acknowledgements.—We should like to thank Mr. G. H. Macnab for permission to publish this case; also Dr. A. W. Morgan for the pathological report and the photomicrographs, and the Photographic Department, Westminster Hospital, for the photographs of the specimens.

REFERENCES

MAJOR, R. H. (1918), *Johns Hopk. Hosp. Bull.*, **29**, 223.
WILLIS, R. A. (1952), *The Spread of Tumours in the Human Body*, 2nd ed. London: Butterworth.

TORSION OF AN HOUR-GLASS GALL-BLADDER WITH FOCAL ARTERITIS

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SECONDARY constriction of the gall-bladder proximal to impacted calculus in the fundus is not uncommon, but as a primary condition hour-glass deformity of this organ is extremely rare. In his comprehensive review of congenital malformations of the gall-bladder Gross (1936) only mentioned one instance; this had been described by Bársony (1927) under the name of 'diverticulum of the fundus'. More recently, Flannery and Caster (1956) recorded another case from their own experience. In Bársony's patient the diagnosis had rested on radiological appearances; Flannery and Caster confirmed their X-ray diagnosis by operation and they found chronic cholecystitis and calculi which were confined to the distal compartment. The following case is of torsion of an hour-glass gall-bladder with focal arteritis.

CASE REPORT

HISTORY.—A 46-year-old staff sergeant was admitted three times over a period of two months, complaining of upper abdominal pain. There had been several similar episodes during the previous year, but these had subsided on bed-rest at home. The pain was colicky and well localized to the right upper quadrant, it was unaccompanied by other digestive, urinary, or general symptoms, and the patient was unaware of any precipitating cause. There was no history of fat intolerance, jaundice, or of loss of weight, and until the onset of his present trouble, he had suffered from no serious illnesses. On each admission the pain rapidly responded to 100 mg. pethidine.

ON EXAMINATION.—Apart from transient slight fever on one occasion, the only abnormality on examination during the attacks was tenderness and guarding, but no rigidity, in the right hypochondrium. Neither the gall-bladder nor the liver edge was palpable. The tenderness disappeared soon after the pain had subsided. Plain radiographs of the abdomen, white-cell counts, and serum amylase estimations showed no abnormality.

Oral cholecystography was inconclusive, but an intravenous cholangiogram clearly outlined two partly superimposed shadows of unequal size (*Fig.* 216). Both segments concentrated the radio-opaque medium well, and emptying was brisk and synchronous. The appearances suggested an unusual type of bilobed or a twisted gall-bladder.

AT OPERATION.—Laparotomy was performed through a midline epigastric incision (J. T.). A circular constriction divided the gall-bladder into a larger proximal and a smaller distal segment. On exposure the distal

FIG. 216.—Cholangiogram, showing two partly superimposed ovoid shadows.

segment was found to be twisted by a full turn around the isthmus. It untwisted readily and its contents were then easily emptied into the proximal compartment and thence into the common bile-duct and the duodenum. Neither compartment contained calculi and no surrounding œdema, congestion, or adhesions suggested recent or chronic inflammation. The remainder of the extrahepatic

biliary tree, the liver, and the other abdominal viscera were normal. A routine cholecystectomy was performed, and from this the patient made a good recovery. He has had no further attacks since the operation.

PATHOLOGY.—Naked-eye examination of the operation specimen confirmed the presence of a constriction about

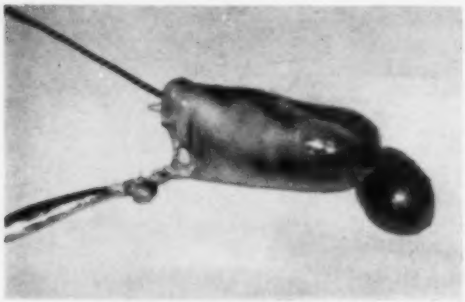

FIG. 217.—The operation specimen, distended with saline. The probe is tied in the cystic duct. The thin fibrous band along the hepatic border is put on stretch by the artery forceps.

1 in. proximal to the tip of the gall-bladder (*Figs.* 217, 218). This was not caused by outside pressure, and there was no obvious scarring. A thin fibrous cord stretched along the hepatic border of the organ from the constriction to the opening of the cystic duct. The twist of the distal segment could be reproduced by filling the gall-bladder with fluid.

Microscopic examination showed a normal mucosa, but one section from a macroscopically normal part showed an area of acute focal arteritis. The vessel involved was a medium-sized arteriole in the muscle-layer; all its coats were infiltrated and its lumen was partly obliterated by inflammatory exudate.

DISCUSSION

Gross (1936) suggested that an hour-glass deformity of the gall-bladder may arise in the same way that atresia is said to develop in the small intestine, i.e., from incomplete resolution of the solid phase through which the viscus passes in embryonic life. A developmental abnormality was certainly suggested in our case by the absence of an obvious primary lesion at the level of the constriction and by the healthy naked-eye appearance of both compartments. The presence of arteritis in another part of the gall-bladder suggests equally plausibly the possibility that a similar lesion had been the underlying cause of the constriction. A variant of polyarteritis, "different from periarteritis nodosa in every respect except the morphological picture", was described by Plaut (1951) in 1·34 per cent of 6576 appendicectomy specimens; and focal non-progressive vasculitis of uncertain aetiology with no systemic manifestations has been found, accidentally or after

FIG. 218.—The operation specimen opened, showing the two compartments, separated by a ridge. The mucosa appears normal.

surgical removal for local symptoms, in most abdominal viscera including the gall-bladder (Kline and Young, 1934; Cottier and Vogt, 1957; Bourne, 1958). Generalized polyarteritis nodosa may also present with abdominal symptoms such as acute cholecystitis (Zeek, 1953; Pugh and Stringer, 1956; Rose and Spencer, 1957; Lee and Kay, 1958), but there was no evidence of widespread disease in our patient at the time of the operation and he has developed no untoward symptoms during the past year.

REFERENCES

BÁRSONY, T. (1927), *Münch. med. Wschr.*, **74**, 546.

BOURNE, W. A. (1958), in *Modern Trends in Gastroenterology*, 2nd Series (ed. F. Avery Jones). London: Butterworth.

COTTIER, H., and VOGT, W. (1957), *Schweiz. med. Wschr.*, **87**, 638.

FLANNERY, M. G., and CASTER, M. P. (1956), *Int. Abstr. Surg.*, **103**, 439.

GROSS, R. (1936), *Arch. Surg., Chicago*, **32**, 131.

KLINE, B. S., and YOUNG, A. M. (1934), *J. Allergy*, **6**, 258.

LEE, H. C., and KAY, S. (1958), *Ann. Surg.*, **147**, 714.

PLAUT, A. (1951), *Amer. J. Path.*, **27**, 242.

PUGH, J. I., and STRINGER, P. (1956), *Brit. J. Surg.*, **44**, 185.

ROSE, G. A., and SPENCER, H. (1957), *Quart. J. Med.*, **26**, 43.

ZEEK, P. M. (1953), *New Engl. J. Med.*, **248**, 764.

SPONTANEOUS RUPTURE OF THE RENAL PELVIS FROM CALCULOUS OBSTRUCTION OF THE URETER

By E. G. HARDY

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THE normal renal pelvis, when distended because of sudden obstruction of the ureter, very rarely bursts. The following example of this unusual complication is therefore reported.

CASE REPORT

A 64-year-old widow was admitted to hospital as an emergency on July 5, 1958. She gave no previous urinary history. Five days before admission she developed pain, not severe, in the right hip radiating to the loin. Three days later the pattern changed to one of pain in the right loin radiating to the right lower abdomen and vulva. At 1 a.m. on the day of admission pain in the right loin, flank, and abdomen suddenly became severe and she vomited. This pain continued with great intensity until operation 19 hours later. There was no history of injury.

FIG. 219.—Post-operative intravenous urography, showing grossly hydronephrotic right kidney.

FIG. 220.—Intravenous urography before discharge 48 days later showing the hydronephrosis to be much smaller.

ON EXAMINATION.—She was in fair condition but in great pain. There was acute tenderness in the right loin, flank, and abdomen, with right-sided abdominal rigidity and rebound phenomenon. The indications for exploration seemed clear, but the provisional diagnoses—high retrocæcal appendicitis or acute perforative cholecystitis—were not held with any confidence. The actual condition found—obvious enough in retrospect—was not considered pre-operatively because it was not known to occur.

AT OPERATION.—Laparotomy through a right paramedian incision revealed no intraperitoneal abnormality apart from a small clear effusion. The retroperitoneal tissues behind the cæcum and ascending colon were boggy with fluid, and exploration through a right paracolic incision quickly disclosed that this was a urinary extravasation. The ureter was at least twice the normal calibre, but flaccid and deflated. Gentle exploration along the avenue of the extravasation led to a longitudinal tear in the anterior wall of the right renal pelvis, extending from the hilum almost to the pyelo-ureteric junction. The kidney and its pelvis were within normal limits of size. There was nothing to suggest that there had been a long-established hydronephrotic sac, although the condition of the ureter indicated that acute hydronephrosis had preceded the rupture.

From these findings, obstruction at the lower end of the ureter was deduced, and was confirmed by passing a ureteric catheter distally. The ureterovesical junction was displayed extraperitoneally through the lower end of the abdominal incision, and a tightly impacted stone measuring $\frac{1}{2} \times \frac{1}{4}$ cm. was removed from the intramural part of the ureter through a ureterotomy, which was then repaired. During this step the ureteric orifice was slit in an effort (vain, as it proved) to prevent later stenosis. The rent in the renal pelvis was repaired with catgut sutures, and remarkable fragility of this tissue was noted at this time. Extraperitoneal drains were placed down to the renal pelvis and the lower end of the ureter—the former through a separate flank incision.

FIG. 221.—Intravenous urography, March 12, 1959, showing mild but static hydronephrosis.

PROGRESS.—Initially, all went well after operation. The drains were both removed by the seventh post-operative day. Leakage of urine from the flank drainage wound gradually lessened and ceased by the nineteenth day. Drying of the fistula, however, was followed by recurrence of pain and the development of an encysted collection of clear urine in the flank. This was drained on the twenty-second post-operative day, and under the same anæsthetic cystoscopy revealed a blockage of the

right ureter 2 cm. proximal to its orifice, due presumably to scarring either from the impaction of the stone or from the trauma of its removal. The obstruction could not be passed with a ureteric catheter or bougie. Drainage of the collection of urine in the flank caused temporary improvement, but although the tube was left in place it drained less and less, and pain and swelling in the loin increased. Intravenous urography showed poor concentration, but it could be seen that the right kidney was grossly hydronephrotic (*Fig.* 219). Quite contrary to reasonable expectation it seemed that the fistula of the right renal pelvis had healed despite the blockage at the lower end of the ureter, and severe renal damage from back pressure was being caused.

Urgent re-operation was performed 29 days after the original exploration. The lower ureter was exposed and found to be distended right down to the ureterovesical junction. The ureter was sectioned flush with the bladder and re-implanted a centimetre or two higher up. The bladder was drained by a temporary suprapubic cystostomy. The patient made a good recovery from this operation and was discharged in good condition and with all her wounds healed 48 days after her first admission. Intravenous urography just before discharge showed the function of the kidney to be good and the hydronephrosis much smaller (*Fig.* 220). The patient remains well, apart from an incisional hernia for which a belt is worn. Intravenous urography on March 12, 1959, showed the kidney to be functioning well; there was still mild hydronephrosis, but this appeared to be static (*Fig.* 221).

DISCUSSION

'Spontaneous' rupture of a hydronephrosis, though rare, is not unknown. Abeshouse (1935) collected 29 examples, and a number have been added since, in the English language literature by Larks (1942), Reid and Menzies (1945), Nyström (1946), and Cowie (1949). Many of the reported cases have been infected, however, and in some the condition has been little more than a uriniferous perinephritic abscess around a pyonephrosis—a technical rather than a dramatic rupture of the renal pelvis.

When a simple, chronic hydronephrosis ruptures, minor or unnoticed trauma may be the cause, so that in some cases the rupture is not truly spontaneous. Larks believes this to be one reason for the diverse incidence of 'spontaneous' rupture reported by different authorities. Nyström, whose own case occurred during pole-vaulting, believes that rupture of a hydronephrotic kidney occurs for the same reasons as rupture of a parenchymatous organ, i.e., external stress or deformation. He thinks that a "hydraulic bursting effect" is unlikely ever to be the cause.

In the case of a chronic hydronephrosis, where accommodation of the renal pelvis has occurred, Nyström's hypothesis is probably correct. Such kidneys at operation are rarely very tense. If hydraulic bursting were ever to occur one would expect it in acute hydronephrosis following sudden ureteric blockage. That this hardly ever happens is presumably due to the bursting pressure of the normal renal pelvis being higher than the back pressure needed to stop the kidney secreting. In the case here recorded, where extreme friability of the renal pelvis was noted and commented on at operation, the reverse may have been the case.

REFERENCES

ABESHOUSE, B. (1935), *Surg. Gynec. Obstet.*, **60**, 710.
COWIE, I. (1949), *N.Z. med. J.*, **48**, 19.
LARKS, G. (1942), *Brit. J. Surg.*, **29**, 354.
NYSTRÖM, T. (1946), *Acta chir. Scand.*, **93**, 513.
REID, R., and MENZIES, W. (1945), *Brit. J. Surg.*, **32**, 491.

REVIEWS AND NOTICES OF BOOKS

Sympathectomy—An Anatomical and Physiological Study with Clinical Applications. By P. A. G. MONRO, M.A., M.D. (Cantab.), M.Sc., Lecturer in Anatomy, The University of Cambridge. 9¼ × 6 in. Pp. 290 + xx, with 84 illustrations. 1959. London: Oxford University Press. 75s.

THIS is an anatomical and physiological study based on the investigation of patients operated upon in the Neurosurgical Department of the London Hospital. The methods used were measurements of electrical resistance in the skin to record areas of sweating after various forms of sympathectomy, and digital plethysmography to estimate the effect of sympathectomy upon peripheral bloodflow. The book contains a great volume of recordings which have been made with exemplary care and completeness—sufficient to justify the author's plea that similar records should be made by others who claim to be publishing the results of operations on the sympathetic system.

He points out that the most "complete" sympathectomy cannot abolish sweating in the 1st and 2nd lumbar dermatomes, which he attributes to the presence of lumbar intermediate ganglia which are not excised; nor in the central area of the face and in the perineum, which may be innervated through the craniosacral outflow of the parasympathetic. This observation removes a great deal of the force of the argument for removing the first lumbar ganglion in order to achieve complete sympathetic denervation of the lower extremity.

Full consideration is given to the problem of the return of sympathetic function after upper limb sympathectomy, and since, if regeneration is the explanation for this, there must be regeneration of preganglionic fibres establishing connexions with ganglion cells, resection should include as much ganglion tissue as possible. Removal of the middle cervical ganglion as well as the inferior is proposed, but post-operative observations are not yet available to show whether this extension of the usual operation is more effective. The few isolated cases reported by the author and by others do not indicate that excision of the middle cervical ganglion makes any appreciable difference.

The author admits the discrepancies which clinicians have observed between the relief of symptoms (especially hyperhidrosis) and the "completeness" of sympathetic denervation; but since this book is a record of clinical scientific investigation rather than of surgical practice, he concentrates quite properly upon his instrumental measurements and not upon their clinical applications, though brief reference is made to these also.

The book is a valuable work of reference for all clinicians and scientists who take a special interest in the sympathetic nervous system. It would have made pleasanter reading had it not been a thesis, if the author

had not felt obliged to refer in so much detail to the publications of numerous other workers, if the clinical records and charts had been placed in the appendix instead of in the body of the book, and if there were not quite so many repetitions, many more than are required for emphasis or for the instruction of even an uninformed reader.

La Biologie des Homogreffes. 9¼ × 6 in. Pp. 284, illustrated. 1959. Paris: Centre National de la Recherche Scientifique. 2200 fr.

THIS volume contains the text and discussion on some twenty of the papers presented at an International Seminar held in Paris in July, 1957, on The Biology of Homografts. The papers are grouped in three sections—the general biology of homografts, homografts and embryology, homografts and immunity—and are based on work carried out by distinguished investigators in Czechoslovakia, France, England, and the United States.

The presentation of the material is admirable and the translators of the original English and American papers into French must be congratulated. A good deal of the work is still in the experimental stage and its interest is rather for the biologist than the surgeon. Although several surgeons have contributed to the volume, the clinical applications of their observations are not clearly stated. There can be no doubt, however, that once the problems of immunity are better understood and overcome, along the lines indicated at this meeting, the transplantation of a very wide range of tissues will be possible.

Although delay in publication may possibly be justified in the case of very large international conferences, it seems a pity that the proceedings of a conference of this type must wait over two years before general release.

Coupes Horizontales du Tronc. By RAYMOND ROY-CAMILLE. 16½ × 12½ in. Pp. 122, with 54 radiographs and 54 schémas. 1959. Paris: Masson et Cie. 8000 fr.

THIS atlas of cross-sectional anatomy comes from the School of Anatomy of the Faculty of Medicine in Paris. It is the result of a study suggested by a leading French radiologist, Dr. Porcher, as a guide to the interpretation of horizontal tomograms. To examine a depth of tissue corresponding to a transverse tomographic 'cut', anatomical sections rather less than 1 cm. thick had to be made. This called for a careful technique of fixation, plastering in correct alinement, and refrigeration before cutting. Fifty-four sections were thus obtained from the trunk of one subject. Radiographs of these closely resemble transverse tomograms. Reproduced alongside each radiograph is a clear line drawing of the corresponding section made by the author's collaborator, M. Delpech. The book is beautifully produced on high-quality paper, and there is a minimum of text. The drawings are adequately but unobtrusively labelled and there is an excellent index. It would be impossible to do justice in a short review to the wealth of detail in the drawings, but an example may be quoted of the instructive sequence showing the lymph-nodes around the tracheal bifurcation and those related to the pericardium and œsophagus.

The author anticipates the criticism that only one subject has been studied by pointing out that the drawings are accurate records and not merely diagrams representing an 'average' of many observations. He reminds us that though there are several well-known cross-sectional atlases they are all based on examination of thicker sections and have correspondingly fewer illustrations.

The work embodied in this book was done under the guidance of the erudite and gracious Professor Gaston Cordier, whose contributions to urgical anatomy are well known. In his preface Professor Cordier expresses the hope that the atlas will be helpful to surgeons. This it can confidently be expected to be, as it not only makes an admirable reference book but offers a rich field for pleasant and profitable browsing. The author and illustrator are to be congratulated on producing a book that may well come to rank among the classics.

Hernia. By Sir HENEAGE OGILVIE, K.B.E., M.A., M.Ch., M.D., F.R.C.S., Consulting Surgeon, Guy's Hospital. 8½ × 5½ in. Pp. 135, with 51 illustrations. 1959. London: Edward Arnold (Publishers) Ltd. 28s.

To be unorthodox is in the Ogilvian tradition. To write interestingly on hernia demands originality and this is certainly to be found in the author's conception of the anatomy of the inguinal canal. When that conception leads to a practical method of operative repair which has apparently stood the test of time, it merits close attention, even if not complete agreement. And, despite the loss of an ancient eponym, the relegation of 'Hesselbach's triangle' to the anatomical waste-paper basket seems sound.

The actual method of repair advocated for inguinal hernia is the narrowing of the internal ring (using linen thread) which is then supported by a musculofascial sling of external oblique. Some fourteen other methods are considered and, with praiseworthy impartiality, for one reason or another rejected.

The treatment of imperfectly descended testis also receives attention, contralateral scrotal anchorage being recommended.

It is unusual and useful to find a description of 'sliding hernia' and its treatment.

For femoral hernia, McEvedy's method is preferred.

It is probably carping criticism to query the initial definition of a hernia as the "displacement of an organ from the cavity in which it is usually contained". Surely there are many herniæ which do not even temporarily contain an "organ"?

This is a comprehensive book, satisfactorily brief, full of much common sense and experience—and not as provocative or controversial as might be expected from its author.

British Obstetric and Gynæcological Practice. Edited by Sir EARDLEY HOLLAND, M.D. (Lond.), F.R.C.P., F.R.C.S., F.R.C.O.G., Consulting Obstetric and Gynæcological Surgeon, London Hospital; and ALECK BOURNE, M.A., M.B., B.Ch. (Cantab.), F.R.C.S., F.R.C.O.G., Consulting Gynæcologist, St. Mary's Hospital, London. Second edition. 9½ × 7 in. Pp. 1228 + xiv, fully illustrated. 1959. London: William Heinemann. 147s.

THAT a second edition of this large and comprehensive work was required in under five years proves its popularity and usefulness. This volume devoted to obstetrics represents the methods and technique of some forty-three authors believed to be a representative cross-section of British obstetricians as drawn from almost all the universities and teaching centres. In spite of the large number of contributors there is very little overlapping in the various chapters. The illustrations throughout this volume are well chosen and well produced; the coloured plates are excellent.

The book is in essence clinical and thoroughly practical, and is designed as a guide for all those interested in practice, including specialists, general practitioner obstetricians, registrars, house officers, and postgraduate students.

An excellent production.

Anatomy of the Human Body. By R. D. LOCKHART, M.D., Ch.M., F.R.S.E., Regius Professor of Anatomy, Aberdeen University, G. F. HAMILTON, B.Sc., M.B., Ch.B., Senior Lecturer in Anatomy, Aberdeen University, and F. W. FYFE, M.A., M.B., Ch.B., Associate Professor of Anatomy, Dalhousie University. Pp. 697 + ix. 1959. London: Faber & Faber Ltd. 105s.

THIS is, in many ways, a unique book, for it presents human anatomy in a simple but very practical way, and students will ever be grateful to Professor Lockhart and his colleagues for writing this excellent volume.

The illustrations, nearly one thousand in all, are excellent, the majority being original, and are beautifully reproduced. The coloured illustrations are simple but very explanatory, and are beyond all praise. There can be little doubt that the old Chinese proverb "a little picture is worth a million words" is well illustrated in this work.

The authors have managed by a simple and direct method of instruction and explanation to cut down the actual text very considerably. By employing a unique arrangement with pointers running from the names in the text to the structures in the figures, less than half the number of words and more than twice the number of illustrations are used in comparison with the standard text-books. This is really a wonderful thing for the medical student of to-day.

Now that this book is published one wonders why somebody did not conceive this method before, because it is simple, instructive, and very practical.

The central nervous system as depicted in this work deserves a special word of praise because it is superbly written and illustrated, many of the drawings being in colour. This section of the book, besides being of real value to the student, will also appeal to neurologists and neurosurgeons.

Professor Lockhart has already published a well-known book on Living Anatomy and, therefore, one would expect the section on surface anatomy to be pre-eminent, and this is certainly the case in this new volume.

Throughout this book emphasis is laid on function and clinical application, so that the book will appeal not only to medical students of all grades, but also to students of physical education, physiotherapy, radiography, and dentistry, and to the clinician.

There can be little doubt that this is the best book on the anatomy of the human body that has so far been produced.

BOOK NOTICES

[The Editorial Committee acknowledge with thanks the receipt of the following volumes. A selection will be made from these for review, precedence being given to new books and to those having the greatest interest to our readers.]

A Text-book of X-ray Diagnosis. Vol. IV. Edited by S. COCHRANE SHANKS, C.B.E., M.D., F.R.C.P., F.F.R., Director, X-ray Diagnostic Department, University College Hospital, London; and PETER KERLEY, C.V.O., C.B.E., M.D., F.R.C.P., F.F.R., D.M.R.E., Director, X-ray Department, Westminster Hospital, London. Third edition. 9¾ × 7 in. Pp. 714 + xvi, with 735 illustrations. 1959. London: H. K. Lewis & Co. Ltd. 110s.

A Textbook of Surgical Physiology. By R. AINSLIE JAMIESON, M.B., F.R.C.S.Ed., Surgeon, Vale of Leven Hospital, Alexandria, Dunbartonshire; and ANDREW W. KAY, M.D., Ch.M., F.R.C.S.Ed., F.R.F.P.S.G., Professor of Surgery, University of Sheffield. 9¾ × 5¾ in. Pp. 623 + viii, with 186 illustrations. 1959. London: E. & S. Livingstone Ltd. 55s.

The Surgeon and the Child. By WILLIS J. POTTS, M.D., Professor of Pediatric Surgery, Northwestern University Medical School, Chicago. 9¼ × 6 in. Pp. 255 + x, illustrated. 1959. Philadelphia and London: W. B. Saunders Co. 52s. 6d.

Transplantation of Tissues. Vol. II. Edited by LYNDON A. PEER, M.D., with twelve contributors. 10 × 6¾ in. Pp. 690 + xiv, with 252 illustrations. Baltimore: The Williams and Wilkins Co. London: Baillière, Tindall & Cox. 160s.

Chirurgisches Nahtmaterial. By HAROLD HUDEMANN, Prof. Dr. Med. Director of the Hygiene Institute, of Medizinischen Akademie, Magdeburg. 9¼ × 6¼ in. Pp. 144, with 35 illustrations. 1959. Jena: Veb Gustav Fischer. D.M. 13.50.

Klinik und Praxis der Urology. Vol. I. By W. STAEHLER. 10¼ × 7¼ in. Pp. 892 + xxiv, with 1034 illustrations. 1959. Stuttgart: Georg Theime Verlag. DM. 240.

Chirurgie der Verengungen der Oberen Luftwege. By AUREL RETHI. 9¼ × 6¼ in. Pp. 119 + viii, with 116 illustrations. 1959. Stuttgart: Georg Theime Verlag. DM. 28.

Die Wirbelsaulenleiden und ihre Differential-diagnose. By J. E. W. BROCHER. 11 × 7¼ in. Pp. 457 + xvi, with 287 illustrations. 1959. Stuttgart: Georg Theime Verlag. DM. 128.

Office Orthopedics. By LEWIS COZEN, M.D., F.A.C.S. Third edition. 9 × 5¼ in. Pp. 430, with 321 illustrations. 1959. London: Henry Kimpton. 70s.

Anesthesia for Infants and Children. By ROBERT M. SMITH, M.D., Anesthesiologist, The Children's Medical Center, Boston, Mass., U.S.A. 9¾ × 6¼ in. Pp. 418, with 182 illustrations. 1959. St. Louis: C. V. Mosby Co. London: Henry Kimpton. 90s.

Color Atlas and Management of Vascular Disease. By WILLIAM T. FOLEY, M.D., F.A.C.P., and IRVING S. WRIGHT, M.D., F.A.C.P. 10 × 7¼ in. Pp. 170 + xiv, fully illustrated. 1959. New York: Appleton-Century-Crofts, Inc. $18.00.

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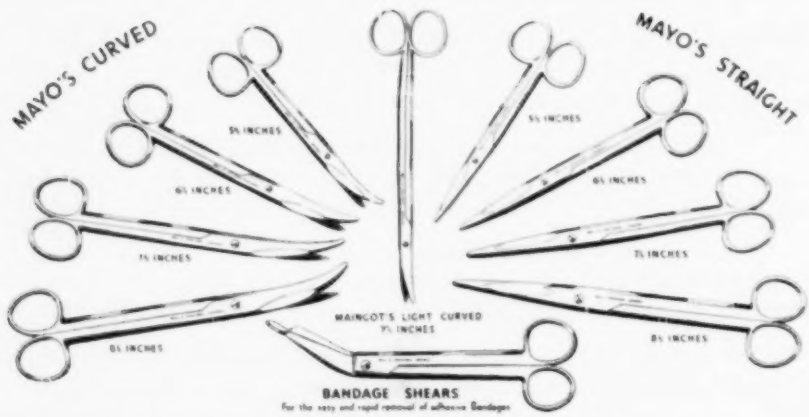

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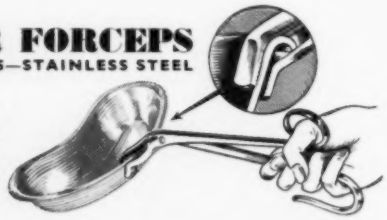

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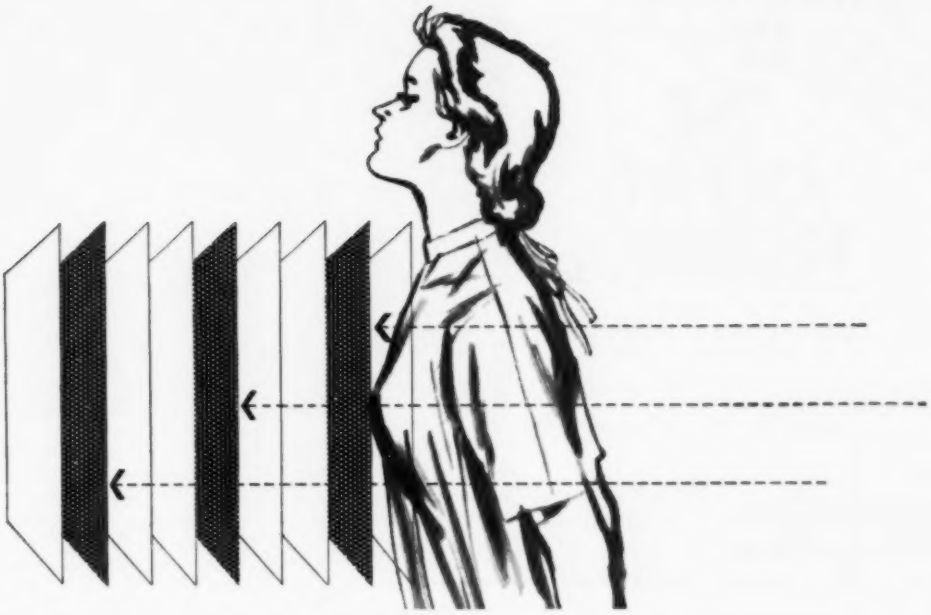

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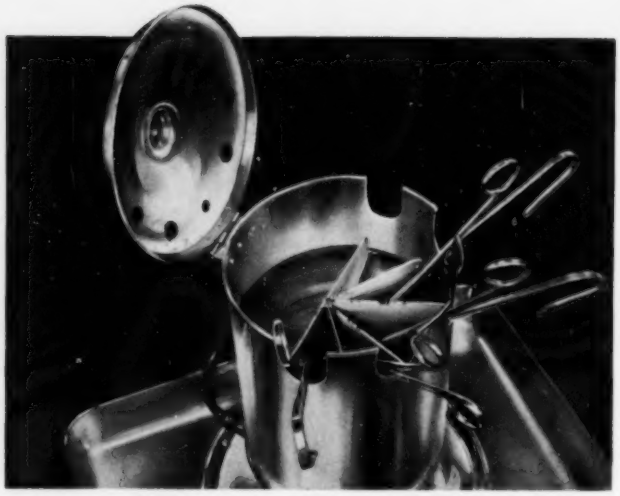

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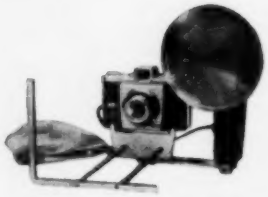

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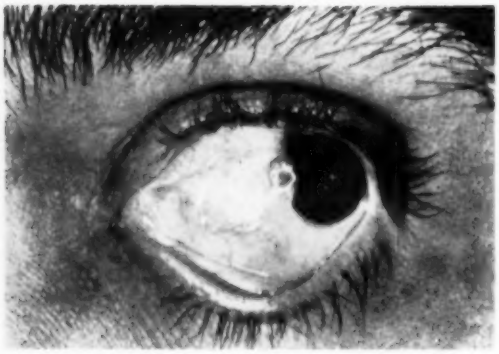

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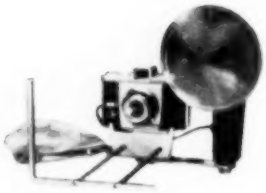

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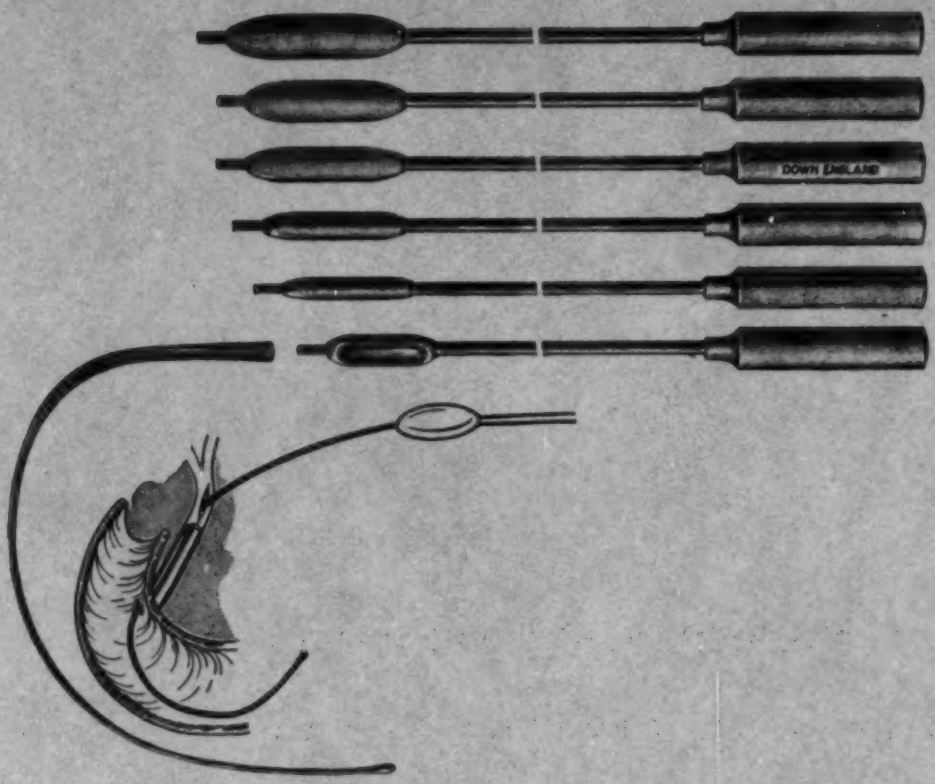

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